VOLUME XV February, 1926 NUMBER 2

Medical Lib
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[FOUNDED IN 1906 AS THE AMERICAN QUARTERLY OF ROENTGENOLOGY]

THE AMERICAN JOURNAL OF ROENTGENOLOGY AND RADIUM THERAPY

OFFICIAL ORGAN
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PUBLISHED MONTHLY FOR THE AMERICAN ROENTGEN RAY SOCIETY
BY PAUL B. HOEBER, INC., 67-69 EAST 59TH STREET, NEW YORK CITY

AMERICAN ROENTGEN RAY SOCIETY MEETINGS

Twenty-Seventh Annual Meeting

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AMERICAN RADIUM SOCIETY

Eleventh Annual Meeting

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Entered as second-class matter, March 3, 1916, at the Post Office, New York, N. Y., under the Act of March 3, 1879.

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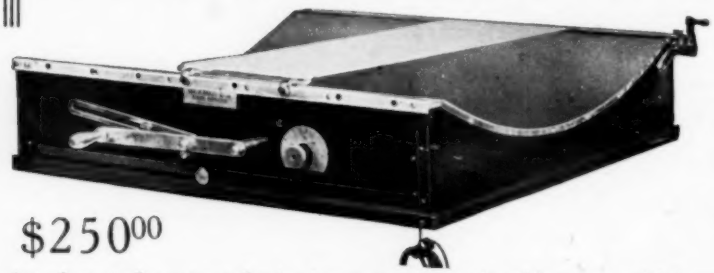

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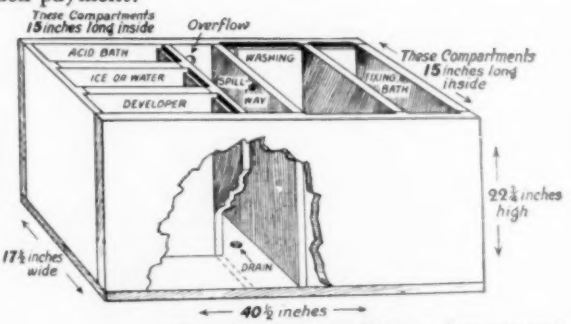

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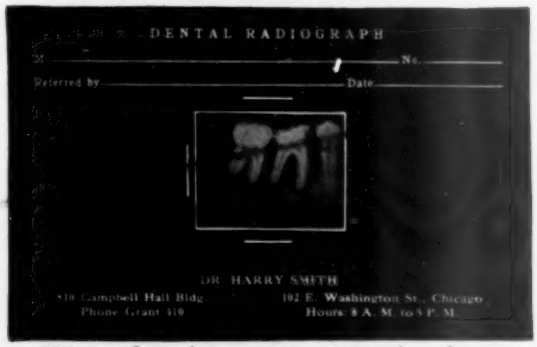

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THE AMERICAN JOURNAL OF ROENTGENOLOGY AND RADIUM THERAPY

VOL. XV FEBRUARY, 1926 No. 2

TISSUE REACTIONS TO RADIATION

CALDWELL LECTURE, 1925*

BY JAMES EWING, M.D.

NEW YORK CITY

IN the development of a new field of scientific research, it often transpires that the main facts are gathered readily and with much precision, while the further effort to pass beyond the line of simple descriptive knowledge and to acquire fundamental explanations of the observed facts meets with insuperable obstacles. Ultimate knowledge of the mode of action of radiation still eludes our grasp. More than a decade ago one could trace in detail the nuclear and cytoplasmic reactions following irradiation, the preliminary hyperemia, cell liquefaction and necrosis, the appearance of phagocytic cells, the growth of granulation tissue, the extreme overgrowth of lymphocytes and plasma cells, the healing by supple scar tissue. The various degrees of susceptibility of normal and tumor tissues were rather clearly understood, and certain general laws of reaction had been formulated. Even the late effects caused by progressive arteriosclerosis were well known and warned against.

The very voluminous contributions of the past decade have served to clarify many details, and the very extensive experimentation by trial and error have shown, to a certain extent, how best to accomplish the desired result, but no new and fundamental principles of reaction have been established, and no illuminating theories have been established. We have become much more practically capable but not much better informed regarding the ultimate nature of the effects of radiation energy.

Owing to the immense importance of correct methods in radiation therapy, it seems worth while to review our knowledge at this time and to summarize the great mass of observations that has accumulated during the past decade, especially with relation to tissue reactions. Owing to the extensive scope of the subject of the physiology of radiation, only a small portion of the topic can be considered at this time.

PRIMARY EFFECTS ON CELLS

Underlying all tissue reactions to radiation are the primary effects upon the tissue cells. While there has been much controversy regarding the relative importance of cytoplasmic and nuclear susceptibility, it must be assumed that both structures suffer together and in varying degree, depending upon the constitution of the cell. No universal rule would seem applicable in this field. The tough cytoplasm of a squamous epithelial cell must resist far more than that of a rapidly growing or embryonal cell, and upon this fact is based the well established law accredited to Bergonié and Tribondeau. That dividing cells are more susceptible than resting cells appears to have been fully attested by experiment and by practical therapeutic test. Here Regaud's well-known demonstration of the capacity of prolonged mild dosage to completely sterilize the testis

* Delivered at the Twenty-sixth Annual Meeting, AMERICAN ROENTGEN RAY SOCIETY, Washington, D. C., Sept. 22–25, 1925.

stands as the foremost evidence of the high vulnerability of mitotic nuclei, but may not perhaps be accepted as proof of the superiority of prolonged dosage. Recently, however, Strangeways has made observations that do not confirm this rule. In tissue cultures of chick embryos he found that small doses of roentgen rays have a definite inhibitory effect, preventing new cells from coming into mitosis, but he could see no evidence that dividing cells were more sensitive than resting ones.

Very varied and interesting are the nuclear changes observed after irradiation, and it may be doubted if sufficient attention has been given to the significance of these variations. On the one hand, we find the enormous swelling and hyperchromatism of epithelial nuclei after large doses of radium. We have no full explanation of this change, which is one of the strictly specific features of the cell damage from radiation. One may suggest that it consists in an imbibition of water by the nucleoproteins, probably at the expense of the cytoplasmic fluids, which are not simultaneously increased. At the other extreme and under conditions not yet set forth, but generally in the case of lymphoid and embryonal tumors, there occur pycnosis, shrinkage and karyorrhexis, which seem to occur mainly when the cytoplasm is hydropic, while the nucleus loses water. All such changes require large doses and when they occur in pronounced form, they seem to assure the immediate or eventual death of the cell.

After full radiation there is always a period during which mitoses are reduced in number or disappear, and when they reappear they are abnormal in form and probably often abortive. According to Alberti and Politzer, in the cornea of the salamander larva, mild radiation (4 H) suppresses mitoses for three or four days and those subsequently appearing are atypical. When a second dosage is given after eighteen hours, the mitosis-free period is lengthened. If the second dose is given after four days, the pathological mitoses fail to appear until after seven days and then they show alterations comparable with those produced by an initial 12 H dose. When the second dose is given after nine days, the effects are equal to those produced by a single dose of 20 H. The authors conclude that the radiation affects not only dividing but also resting cells. Their results strongly favor the method of fractionated dosage. We have, however, no observations on the period when mitoses reappear in tumors in which they have once been suppressed by radiation. The period must vary from days to months, according to the character of the tumor and dosage given. Such observations might become the basis of a more rational therapy.

After single erythema doses, Schreus finds that amitotic division of nuclei largely replaces mitotic division.

That cells may recover from the nuclear damage is attested by the frequent recurrences developing after prolonged irradiation. Indeed in over-irradiated scar tissue, the tumor cells may become extremely resistant; no mitoses nor cytoplasmic changes whatever may be detected over long periods and yet eventually growth capacity is restored.

Regaud conceives that in every tumor there are mother cells which are the only ones capable of multiplication, while others become differentiated and incapable of growth. The principle that certain cells of an organ are set aside for growth and others for function is sound. The germ center cells of the lymph follicles, the basal epidermal cells, and those at the bases of intestinal crypts are examples, but that there is such a physiological division of labor in malignant tumors may be questioned for most cases, and denied for many. In anaplastic tumors, all cells seem to participate in the rapid growth process. Regaud's observations apply mainly to squamous cell carcinoma in which there is a strong tendency toward differentiation and quiescence. Growth capacity is probably long retained in differentiating squamous cells, and they may at a late period become mother cells. In the so-called transitional cell type of epidermoid carcinoma, such as arises from tonsil, nares and gland ducts, there is little tendency toward differentiation. Mitoses appear uniformly throughout

the tumor and these tumors are highly susceptible to radiation. Observation of such tumors leads me to conclude that the action is quite as much upon the more delicate cytoplasm as upon the nuclei, dividing or resting. Here is probably an example of a highly susceptible cytoplasm, since these tumors may, by external irradiation, be reduced to a granular necrotic mass.

Following the interstitial use of platinum filtered needles containing considerable amounts of radium (10–100 mg.) nuclear changes occur in very pronounced and bizarre form and indicate that this method of treatment is capable of sterilizing tissues over a wide area.

The different types of tumor tissue present very different nuclear changes. In lymphomatous processes the very abundant nuclear material rapidly breaks up into granules which are distributed in the tumor fluids and even, as Warthin has shown, may be disseminated throughout the organs. That these nuclear derivatives ever give rise to intoxication has never been proven and seem to me unlikely. Bulky lymphosarcomas melt down in a few hours without any sign of intoxication. On the other hand, in many tumors the amount of nuclear material is comparatively small and nuclear changes occur slowly. During mitosis one may not assume that the effects are solely upon the dividing nucleus. Mitosis is accompanied by marked changes in the cytoplasm which becomes clear and hydropic. In this condition the cytoplasm must be particularly susceptible. Mallet has collected considerable evidence purporting to show the intervals during which mitoses occur in all the cells of a given tumor, and would establish a so-called karyokinetic index. This ambition can probably never be successfully accomplished. There are very wide variations in this respect in different tumors. Moreover the same tumor may show successive periods of growth during which mitoses are very much more numerous than in resting periods.

Bacterial infection greatly stimulates the division of many tumor cells, but does not render the tumor more susceptible to radiation. I have seen clumps of polynuclear leucocytes in cervical carcinoma surrounded by an almost complete double ring of mitotic tumor cells, while more distant tumor areas, free from leucocytes, showed no mitoses. Streptococcous infection is a real and frequent stimulus to the growth of squamous cell carcinoma and cannot be controlled by radiation. The mitotic cells may be very susceptible to radiation, but the infection seems to interfere with the tissue repair induced by radiation and destroys the normal resistance of the tissue while poisoning the host. This element in prognosis is far more important than exact dosage or the relative susceptibility of cytoplasm and resting or dividing nuclei and is the cause of many failures to cure epidermoid cancer.

THEORIES REGARDING THE NATURE OF THE ACTION OF RADIATION

Scientific curiosity leads us to inquire more and more minutely into the ultimate nature of the action of rays upon tumor and tissue cells, but as the inquiries become more fundamental, and the results are phrased in terms of chemistry and physical chemistry, they become less satisfying from the biological standpoint. Since tissues are not merely aggregates of cells but are highly complex systems of related and interdependent structures, purely chemical or physical data can never explain their behavior. Nevertheless much interest and possibly considerable importance attaches to the various fundamental theories and observations regarding the ultimate mode of action of radiant energy.

One of the most obvious and clearly attested of these physical phenomena is an increased permeability of the cell membrane and probably also of the nuclear membrane. The marked swelling of irradiated nuclei and the ballooning of the cytoplasm are most easily and probably correctly interpreted as an increased capacity of these structures to absorb water through an altered cell membrane. The nature of this cell change escapes us, but again assuming the simplest cause, one must suppose that intracellular chemical changes produce new electrolytes by decomposition of salts, proteins and fats, and that water is drawn in by

simple osmosis. The time required to produce these chemical changes may be an element in the latent period following irradiation, which is dependent on the dosage. I know of no data which demonstrate the nature of these chemical changes. It is surprising that there are no simple chemical studies comparing normal tumor tissue with heavily irradiated tumor tissue. If morphological interpretation may be trusted the cell changes mean mainly proteolytic cleavage and autolysis.

Cell ferments, however, seem to be generally inhibited by radiation and the cell metabolism reduced or brought to a near standstill. This fact must be considered when one assumes that successive irradiations act upon increasingly susceptible cells. On the contrary the first exposure may, and probably does reduce the metabolic activity of the cells and render them less susceptible. If the second exposure proves more effective than the first, it must be referred to other factors than increased susceptibility of the cells. Hussey found that a simple system, such as a solution of trypsin or pepsin, is inhibited in action and the ferment destroyed when exposed to considerable amounts of radium. The effect in these experiments was due mainly to the beta rays.

Interesting are the results of Warburg, Negelein and Posener, and Händel and Tadenuma, who show that radiation reduces the capacity of tumor tissue *in vitro* to split glucose into lactic acid and thus, as they conceive, prevents the poisoning of tissues and host by this latter agent. But these observations do not serve to explain the degenerative changes in cells due to raying. According to Roffo cholesterin is split by radiation, but there are contrary observations. The discussions of ionization of cell constituents have not greatly elucidated our problem. Dessauer's theory that radiation produces in the cell points of heat and coagulation from which the effects flow, even if correct, cannot possibly identify irradiation of tissues with the heating of tissues. Fernau considers at some length the significance of increase in the H-ion concentration, modifications of osmotic pressure, changes in the permeability of cell membranes, alterations in the dispersion phase and of the electric charge of colloids, disintegration of lipoids, and changes in the albumins of the plasma, and concludes that none of these factors explain the action of rays. However it may at least be asserted that these observations are probably laying the basis for an eventual solution of the problem. We must therefore conclude that the ultimate nature of the action of rays upon cell structures has not been explained by physics or chemistry and that we must be content, for the present, to interpret the changes in terms of ordinary cytology, which is, however, an extremely precise science.

PHYSIOLOGICAL ACTIONS

Accordingly we turn with relief to physiological considerations. The first of these to which attention may be drawn is that tissues irradiated in the body behave differently from tissue fragments or cells irradiated *in vitro*. Animal tissues are very complex and their reactions depend not merely upon changes in the predominating cell, but upon the integrity of blood and lymph circulation, nerve supply, and other intercellular relations, constituting the environment. Jolly and Lacassagne found only 400 leucocytes per c.mm. in the blood of an irradiated rabbit, but in the blood *in vitro* irradiated with much larger doses there was no reduction in the number of cells or in their ameboid activity.

Giraud and Parès conclude that these results are due not to the direct destruction of the leucocytes by the rays but to the action of leucolytic substances which enter the circulation of the irradiated animal. It is futile to argue from experiments *in vitro* what radiation will do to tumor cells in the body. Otherwise an end would have come to radiation therapy years ago when Wood showed that seven times the erythema dose was required to kill certain mouse cancer cells *in vitro*. The differences in the two modes of experimentation have been fully pointed out by L. Loeb. He emphasizes especially the difference in secondary and scattered radiation *in vivo*, but I think the inflammatory reaction excited in the living tissues is more important.

Since 1907 G. Schwarz has pointed out that the susceptibility to radiation is in direct proportion to the growth metabolism of the tumor cells, while the metabolism devoted to specific function is less important. *In vitro* the metabolism of the tumor cells is probably extremely low, so that they become very resistant to radiation, which acts more effectively the higher the metabolism of the cells. We must therefore look for the explanation of cell changes not merely in the cell itself but in the tissues and even in the body as a whole. This conclusion, now generally adopted, represents the chief progress in radiation physiology of the past five years, and takes radiation therapy out of the field of physics and chemistry and places it in the domain of pathology and medicine. The tissues and the body react to radiation as a whole.

Among the tissue reactions which have always appeared to be most significant are the changes in blood vessels, of which the external evidence of initial hyperemia followed later by induration and relative anemia bear simple witness. The initial hyperemia seems to be merely a somewhat peculiar inflammatory process with vasodilatation, exudation of serum, leucocytes and, especially after roentgen rays, red blood cells. There can be little doubt that these inflammatory changes initiate and determine, to a large extent, the changes in tumor cells, stroma, and blood vessels of the affected part. Again ultimate factors escape us but we can observe cytoplasmic and nuclear hydrops and cell disintegration and observe attack by lymphocytes and plasma cells. We note swelling and mucinous degeneration of collagen fibrils, occlusion and rupture of capillaries with swollen endothelium; in a word, tumor cell damage and stimulus of physiological repair processes in the normal tissues.

The importance of vascular changes following irradiation in the destruction of cancer has surely been underestimated. The nutrition of many tumor tissues is abnormal and highly unstable. It would be interesting and profitable to trace the blood supply of the various tumors, especially those susceptible to radiation. In squamous cell and glandular carcinoma, infiltrating cell groups are nourished by the fine vessels of the invaded tissue and these tumors are resistant. Most tumor cells grow under pressure and very slight increase of pressure is sufficient to strangle tumor masses under many circumstances. Thus encapsulated cancerous lymph nodes become tensely swollen by the contained growth and hence we see a limit of growth, necrosis, calcification, and harmless encystment, in the natural course of some squamous cell carcinomas. Under irradiation the blood supply is cut down, the capsule fibrosed and the necrotic and fibrous processes initiated by doses which are incapable of destroying infiltrating tumor cells. I have observed complete necrosis of transitional cell and of squamous cell carcinoma in cervical lymph nodes by external irradiation, which seems explicable only as the result of strangulation of the blood supply. When, however, these cells rupture the capsule and escape into the tissues no amount of external irradiation seems to control them. That radiation actually closes blood vessels, fine ones at first, large arterioles or arteries later, is attested by the vacuolation and swelling of endothelial cells, beginning in the latent period. Holfelder describes rupture of capillaries, hemorrhage, thrombosis, compression of capillaries by exuded lymphocytes and plasma cells, and growth of new connective tissue, swelling of all coats of large arteries, late arterial sclerosis, and the anemic condition of the radiation cicatrix. Pursuing these threads of evidence in the examination of irradiated tumors, I have become convinced that practical irradiation acts very largely through vascular disturbance. This is one of the main reasons why tumor tissues behave differently in the body than in the test tube. Changes in the lymph flow probably play a similar rôle but are more difficult to follow. The radiation effects are therefore direct and injurious upon the tumor cells and indirect and destructive through secondary factors. These effects require time for their evolution and expression.

Following irradiation there is a latent period in which no gross effects are

observed. This period varies considerably and with the hardness of the rays and the mildness of the dose. It is extremely short (a few hours) with large doses of filtered radium. Even with mild doses Holfelder finds very early swelling and vacuolation of cells. All pathological processes take time to display the effects of disturbance in the life processes of cells. Even necrosis is a necrobiosis. It is the peculiarity of radiation that its effects are fundamental, slow to develop, but persisting through generations of cells, and transmissible to the offspring. That the effects are always deleterious to the cell, are followed by degeneration, but may be succeeded by regeneration, seems to be more firmly established by the observations of the past few years, notwithstanding a few apparently contrary data obtained with plant cells.

Caspari presents some pertinent comments and observations on the question of the stimulating effects of radiation. With relatively small doses, 1 HED in mice, he never saw any acceleration of growth beyond the usual variations. With larger doses, however, 2–2½ HED, he often observed increased growth, although the same doses usually cause immediate regression of the same tumor. The increased growth he would refer to the disturbance of the general resistance of the animal and not to direct effect on the tumor cells. This interpretation is supported by the fact that with extremely large doses, 7 HED, while most of the tumor mass was destroyed, from the remnants there at times developed an extremely rapid, explosive, and bulky growth. Here it must be assumed that the heavy dosage destroyed the local defense mechanism. That a temporary excitation of function, occasionally accompanied by slight growth stimulus precedes the inhibitory effects of radiation, is indicated by the results of Halberstaedter and Wolfsberg, and Piccaluga, on the capacity of irradiated tissues to reduce methylene blue; by the observations of Gutzeit on the increased production of acid by *B. coli;* but none of these observations seems to bear directly on the question of stimulation of tumor growth by therapeutic radiation.

Czepa, after a very full consideration of the data relating to the stimulating effects of small doses of roentgen rays, the Arndt-Schultz law, concludes that these effects when present are probably always due to secondary factors, especially to general action on the body, while the direct action of the rays is always inhibitory.

REPARATIVE PROCESSES

Following the damage inflicted by the rays, there follow regeneration and repair. To this field we must look for a large share and the determining portion of the cure of cancer by radiation. The factors involved in the repair process are very numerous and complex and their effects differ from those observed in other pathological processes. Nevertheless they vary so much from the usual reaction to injury as to constitute a specific set of reactions. The tissue irreactions, following irradiation, offer many illustrations of Weigert's law, that the reaction to injury may be excessive. Indeed when we include carcinoma from roentgen burns and sarcoma in irradiated tuberculous joints, the most bizarre illustrations of Weigert's law must be conceded to the field of the pathology of radiation.

Lymphocytic exudate is one of the earliest and most constant of the repair phenomena. Lymphocytes gather in inflamed tissues as the result of lymph stasis. While these cells are probably not ameboid it is difficult to escape the conclusion that nature has forces to attract them to the field of degenerating tissue cells or other organized or chemical irritants of a low grade. From the earliest days of the microscope, pathologists have observed the accumulation of lymphocytes about the growing edges of cancer in all stages and have assigned to them a protective rôle. There is no doubt that complete destruction of tumor cell foci may follow the accumulation of lymphocytes, that this process is more pronounced in cancer resisting subjects, may be entirely absent in non-resistant subjects, and that it may have a limited clinical prognostic significance as claimed by MacCarty.

It remained for Murphy to emphasize the importance of the lymphocyte in the limitation of the cancer process, in radiation therapy, and in a series of studies he has shown that the effects of radiation therapy depend much on the mobilization of lymphocytes. I think, he has succeeded in proving that the lymphocyte production may be increased in animals by moderate radiation, but must question some of the evidence adduced in favor of this view. Proliferation of germ center cells in lymph nodes probably does not signify increased production of lymphocytes. Most of the modern study tells against Flemming's theory of the origin of lymphocytes from reticulum cells, and the recent popularity of the theory of a distinct physiological unit in the reticulo-endothelial system tells in the same direction. Yet I think Murphy's claim must be accepted that radiation acts partly through the increase and mobilization of lymphocytes, general and local. Autopsies on cancer subjects generally reveal a notable diminution or even comparative absence of lymphatic tissue. Whether the initial impulse to attack cancer cells resides in the lymphocytes, or whether they gather mechanically about degenerating tumor cells, through closing lymphatics, we do not know, but that this gathering is often followed by atrophy of the tumor cells and that this process may be stimulated by radiation, are facts of importance.

The lymphocyte works not only in companies but with greater power in the organized structure of the lymph node, which is the great barrier against dissemination of cancer. The behavior of lymph nodes is of great importance to radiation therapy and is subject to some peculiarities which seem thus far to have escaped general attention. First of these is the marked resistance of *normal* lymph node tissue to radiation. While tumors of lymph nodes, both lymphocytoma and reticulum cell sarcoma, melt down rapidly under radiation, probably owing to vulnerability of dividing cells and instability of nutrition, simple hyperplasia, such as of tonsils, requires large doses before yielding, and normal lymph nodes I find comparatively resistant. After extremely heavy external irradiation, two hours' high voltage roentgen rays and two 10,000 mc-hr. radium-packs, squamous carcinoma cells may be found necrotic while lymph follicles persist or even increase in number and a thick rim of lymphoid tissue remains beneath the capsule of the distended node. An example of lymphoid hyperplasia existing one month after very heavy irradiation is illustrated in Figure 1. In a series of lymph nodes receiving heavy irradiation, somewhat less than the above case, I have observed the following changes: (1) the transformation of the germ center into a small compact ring of flat cells resembling squamous epithelium; (2) replacement of the germ center by lymphocytes; (3) obliteration of follicles but persistence of lymphocytes; and (4) reticulum cell hyperplasia.

Some of these changes generally follow the delivery of 80 min. high voltage roentgen rays, and 10,000 mc-hr. of radium, but recovery apparently follows after three or four months or less, and may be succeeded by lymphoid hyperplasia. The lates equels of this heavy irradiation have not been determined.

As pointed out by Quick and Cutler, these observations encourage the preservation of lymph nodes in the neighborhood of squamous cell carcinoma, when not invaded, and their heavy irradiation when they are invaded. They further widen the breach between those who extirpate normal cervical lymph nodes in 60 per cent of the cases of lip carcinoma, and the radiologist who conserves these barriers against cancer extension when uninfected, and plans to control them when infected. Owing to their cellular structure and rich blood and lymph supply, lymph nodes seem to be particularly capable of responding to radiation by extreme and effective cellular reaction.

Plasma cell reaction, sometimes in quite excessive degree is, under many circumstances, one of the characteristic features of radiation repair. It is found particularly in the cervix uteri after heavy caustic dosage and again in heavily irradiated lymph nodes. I have come to regard it as of distinctly favorable import and in its excessive degree it must be regarded as

specific of radiation healing. It may occur with or without lymphocytes but is not sufficiently connected with lymphocytes to strengthen the theory of the origin of plasma cells from lymphocytes. The fact that one never sees cancer cells growing out into a field of plasma cells indicates that these cells, or the conditions in which they occur, are highly antagonistic to the cancer process. Like the lymphocyte they persist and multiply freely in heavily irradiated lymph nodes and probably in other tissues if the blood supply is not deficient. Unless the plasma cell is derived from the endothelial tissue leucocyte, I do not find that the latter cell is prominent in radiation healing. It may take part in the formation of giant cells and foreign body tubercles which frequently form in the late stages of tumor regression, and may closely resemble those of true tuberculosis.

Connective tissue appears in the healing process under many circumstances. It represents the end product of all the cellular reactions, when it may have very scanty bulk and few or no cells. Very cellular connective tissue with considerable growth momentum develops in irradiated lymph nodes, muscles and subcutaneous tissue. One can usually trace the connective tissue reaction to marked injury and degeneration of normal connective. After heavy roentgen-ray dosage, one finds mucinous degeneration of collagen fibrils, fragmentation of fibers, hemorrhage from ruptured capillaries and then actual growth of fibroblasts. In some irradiated lymph nodes the connective tissue reaction has approached the grade of fibrosarcoma.

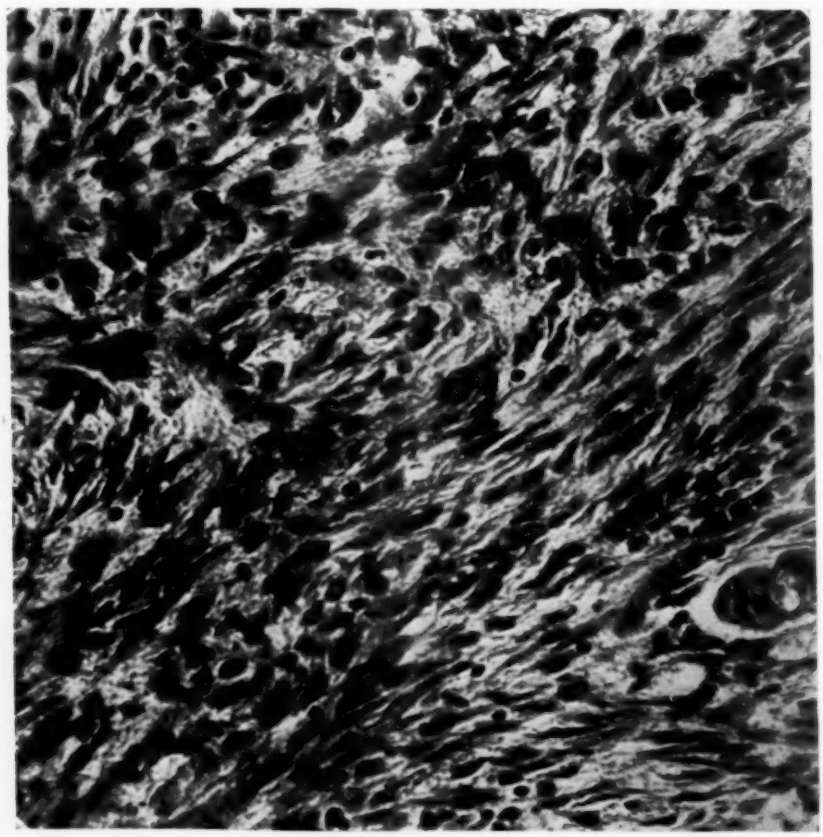

FIG. 1. 8398. Extensive cellular hyperplasia, resembling sarcoma in a heavily irradiated lymph node invaded by squamous cell carcinoma. High voltage roentgen rays, 80 min., on both sides of neck, three months, two months, and two weeks before operation. Radium 8000 mc-hr. one week before operation.*

*The high voltage roentgen-ray treatments and the radium packs used in the cases referred to in the text and in the illustrations consisted of the following elements:

Radium Pack: Two grams of radium distributed over an area 7 × 10 cm. Filter, 2 mm. brass, at a distance of 6 cm. The erythema dose is 10,000 mc-hr.; at 10 cm. it is 20,000 mc-hr.

High Voltage Roentgen Rays: Voltage, 200 kv. peak; filter, 0.5 mm. copper, 1 mm. aluminum. Target skin distance, 50 cm., 4 ma.; time for erythema dose, 80 min.

Especially in deep radiation therapy, the connective tissue reaction and overgrowth seems to be very prominent and to increase, out of proportion to the damage to tumor cells. In 1909, Caan after apparently rather weak doses, found no changes in deep-lying tumor cells until after ten to twenty days, while growth of connective tissue began at once, necrosis of tumor cells and leucocytic invasion coming at the end of the healing process.

True sarcoma has been produced experimentally in animals from roentgen-ray injuries. I have seen one case of large spindle cell sarcoma developing after some years in a leg repeatedly irradiated for osteogenic sarcoma. It was not clear whether the sarcoma developed from muscle cells or fascial tissue. Five cases of sarcoma, type not stated, are reported by Beck from roentgen-ray treatment of tuberculous joints.

New capillaries often develop in the connective tissue, producing the ordinary granulation tissue of healing wounds. At times the capillaries grow actively and are effective weapons in excavating and destroying the tumor cells. Through the kindness of Dr. Klemperer, I have studied one case of recurring capillary angiosarcoma developing on a roentgen ulcer.

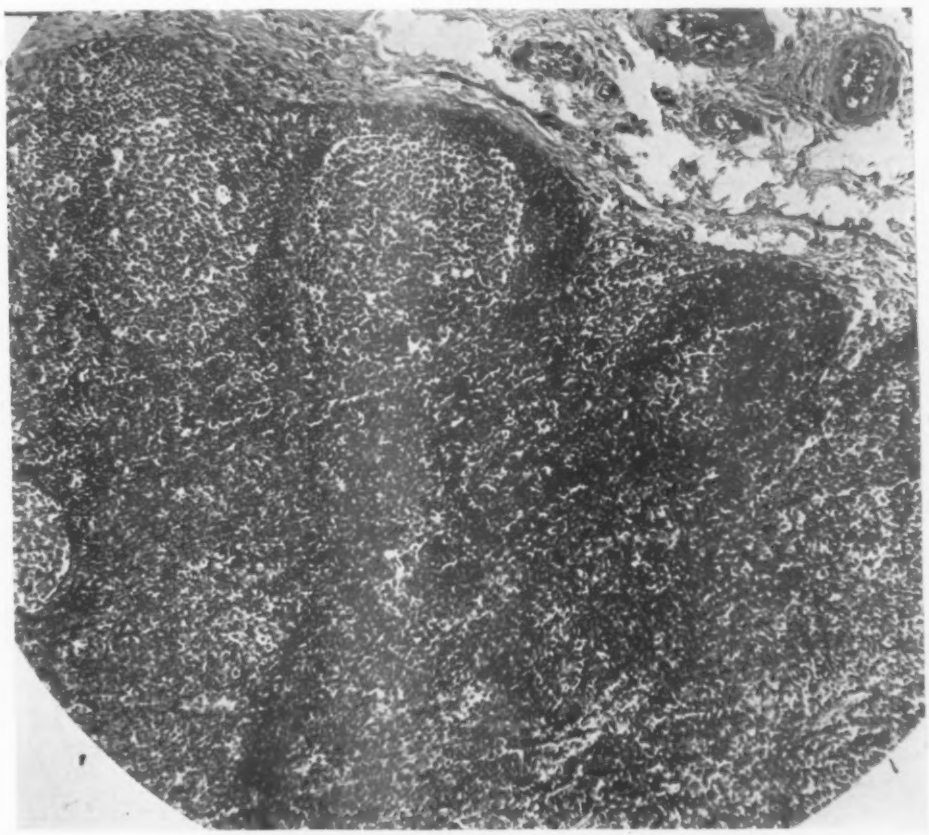

FIG. 2. 8636. Structure of lymph node after heavy irradiation. Persistence of lymph follicles, mitoses in reticulum cells, and lymphocytic hyperplasia. High voltage roentgen rays, 80 min. on both sides of neck, two months and one month, and radium pack 10,000 mc-hr. on both sides one month before removal.

Abortive fibrosis (Fig. 4) is a term that may be applied to a form of indolent fibrosis with destruction of all tissue cells and most blood vessels, but persistence of tumor cells. It occurs after repeated and excessive irradiation and probably more often after radium than after roentgen-ray treatment. It is one of the common end products of unsuccessful irradiation. It

presents wide hyaline strands of fibrous tissue inclosing groups of well preserved tumor cells. The blood vessels are scanty but some rigid sinuses usually persist, maintaining the nutrition of the tumor cells. In such tissue no reasonable amount of radiation seems capable of killing the tumor cells which have acquired an increased resistance greater than that of the normal tissues. The normal relations are thus exactly reversed. The resistance, however, is probably more apparent than real, for incased in dense fibrous tissue, the tumor cells are protected from any attack by defensive cells. Abortive fibrosis can be prevented only by avoidance of overdosage and the only remedy is extirpation of the tissue.

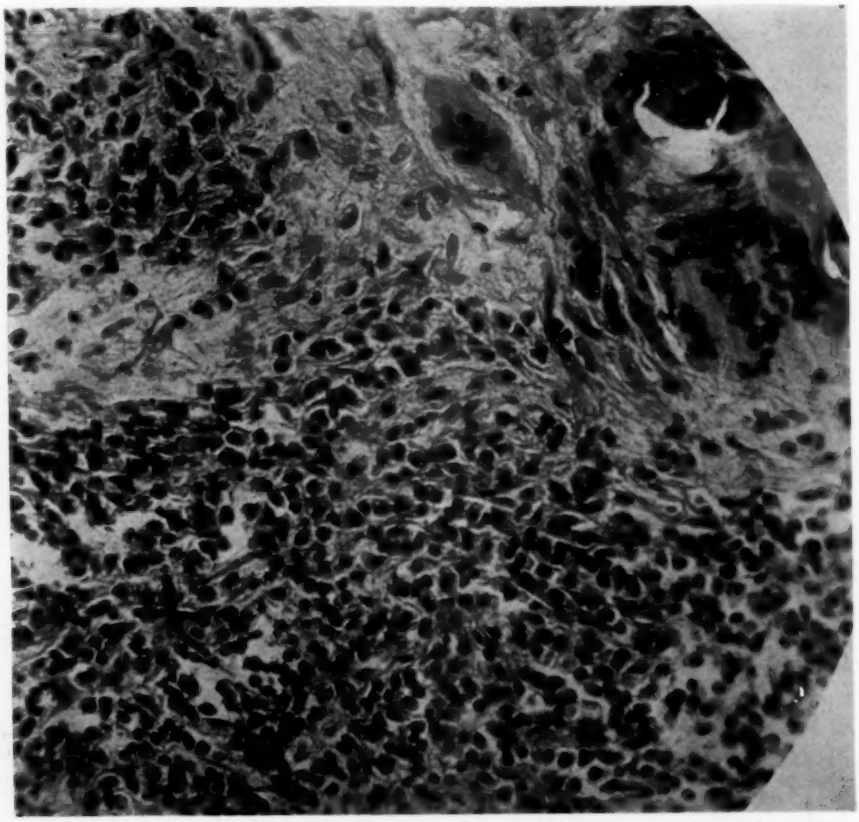

FIG. 3. 8721. Reaction in lymph node after heavy irradiation. Rich plasma cell exudate. Necrosis and calcification of squamous cells. Giant cell formation. High voltage roentgen rays, 80 min., twenty-one, fourteen and six days on tumor side of neck, and nineteen and four days on opposite side, before removal. Radium 10,000 mc-hr., three days and one day before removal.

The *reactions of fat tissue* are marked by several peculiarities, which are of much importance in the prognosis of many cancers and especially mammary cancer. Fat tissue with the low metabolism of fat deposits is highly resistant to radiation, but after heavy dosage the cell membranes rupture, minute oil cysts form, saponification occurs, new blood vessels appear, and considerable proliferation of the fat cells may occur. All this forms a poor defense against cancer cells which are difficult to destroy when invading fat tissue, again illustrating the dependence of tumor regression upon the activity of tissue cells. The resistance of mammary cancer in breast and axilla seems to depend mainly upon two factors: (1) the feeble development of axillary lymph nodes, and (2) the abundance of fat tissue into which the tumor cells may freely grow and escape the usual attack by lymphocytes.

Axillary lymph nodes are not fixed anatomical structures. They come and go, and in mammary cancer subjects they are generally scanty. Unlike the cervical nodes they may lack a complete capsule. When invaded by cancer the cells pass readily through the wide lymphatic channels to the next node and they easily pass the fenestrated capsules and invade the fat tissue. Hence radiation, like surgery, has a difficult problem in controlling mammary cancer and its axillary extensions, especially in fat subjects. By external irradiation it is difficult to excite an adequate cellular reaction in axillary fat tissue. Thorough interstitial irradiation by needles would seem to be the only adequate method of exciting the fat tissue to vigorous response, and in some cases it has been found effective.

Bone tissue is peculiar in structure and composition and its reactions form a very special chapter in our topic. Bone is nourished largely by the periosteum, partly by nutrient arteries and capsular arteries about the ends of long bones. Its nutrition depends partly on that of the bone marrow. Haversian branches incased in bone lamellae furnish fluids to the bone cells which lie in very numerous lacunae communicating by fine canaliculi. Bone tissue has a high proportion of calcium, atomic weight 40, which produces an unusual degree of secondary radiation. Bone is a relatively resistant tissue, but this limit is often passed in therapeutic radiation. Everyone knows, too often from experience, that bone must be avoided in the use of interstitial irradiation, otherwise extensive necrosis with very slow and painful sloughing

FIG. 4. 10542. Abortive fibrosis in endothelial myeloma. Persistent rich cell masses without mitosis two years after irradiation. Four radium treatments, 10,000 mc-hr. each.

and infection results. Marked delay in the healing of fractures after moderate irradiation has been recorded by Cluzet.

Experience in the treatment of bone sarcoma shows that the normal bone resists all but very heavy irradiation, but begins to show damage when high voltage roentgen rays are used for five or six hours. These doses generally produce thickness. Meantime the bone marrow is deprived of marrow cells and is reduced to an ill nourished mass of mucinous fat and fibrous tissue. I have an impression that under the above dosage the whole exposed shaft may become practically dead, although functioning, and that about it a new involucrum must eventually form if the bone is to be restored. In the

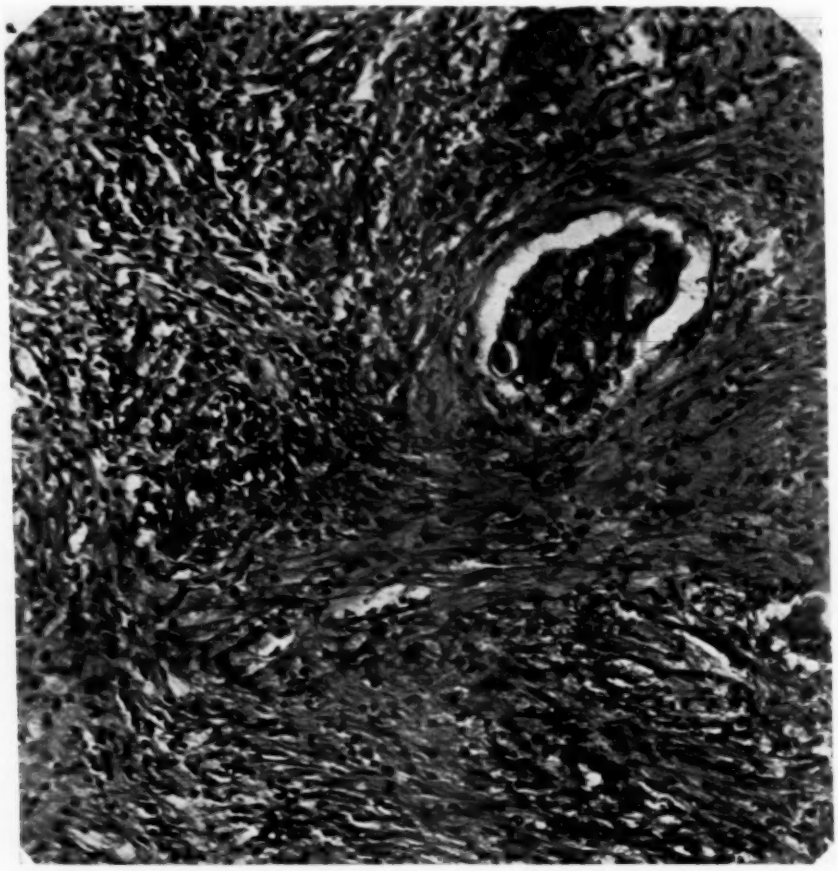

FIG. 5. 8845. Regressing squamous cell carcinoma in lymph node. Marked growth of cellular connective tissue with lymphocytes. Various stages of degeneration and absorption of tumor cells. High voltage roentgen rays, 60 min., fifteen days and six days before removal. Radium 9000 mc-hr. one day before removal.

much growth restraint with ossification, necrosis, and hemorrhage in sarcoma tissue. The danger in this procedure is the incitement of a chronic productive radiation osteitis. In this condition the bone becomes very hard and brittle, spontaneous fractures often occurring; the periosteum becomes thickened and hyaline, points and flakes of necrotic bone appear, and the shaft may be greatly increased in treatment of bone tumors, primary or secondary, one cannot rely upon much cellular reaction, except perhaps in wide areas of marrow, but must proceed on the principle of growth restraint. That this therapeutic principle is safe and may lead to success is attested by the remarkable degree of ossification produced in many osteosarcomas, by the occasional radiation cure of these tumors, and by the extreme

osteoplastic tendencies developed in metastatic carcinomas. Ginsburg has reported an extreme case in which nearly every bone in the body was the seat of metastases, which under irradiation caused great thickening from new bone, while the patient remained for several years in a fair state of health. I know of no better example of the importance of adopting the principle of growth restraint when the attempt at tumor destruction would have been disastrous.

THERAPEUTIC METHODS AND DOSAGE

How may these radiation effects best be secured for the cure of cancer? It cannot be said that the vast amount of experiment, practical experience, and debate of the past decade permits an answer but it is apparent that the question is becoming gradually narrower and the contending views less numerous. With the more definite formulation of principles and theories the final solution will be hastened. Already certain sophistical theories and bad practices have been abandoned. Krönig and Seitz' outspoken view regarding a killing carcinoma and sarcoma dosage has been drowned in a chorus of protests. Nevertheless it is possible that the pendulum has swung too far from the large single effective and in a sense "killing" dosage. From all quarters evidence has accumulated in favor of the view that the body, as a whole and the affected tissue in particular, must be relied upon to accomplish the cure of malignant tumor under irradiation. In this field Murphy's experiments with Nakahara and others must now be regarded as decisive, when he showed that the typical regressive changes in tumor and tissue could be induced by irradiating the soil or the whole animal previous to the implantation of tumor fragments. Lacassagne and Samssonow report results with a rat sarcoma which they state do not support Murphy's observations. Yet the protocols of these experiments show very irregular results with this particular tumor. In many instances the grafts failed to grow or soon regressed when planted in irradiated soil.

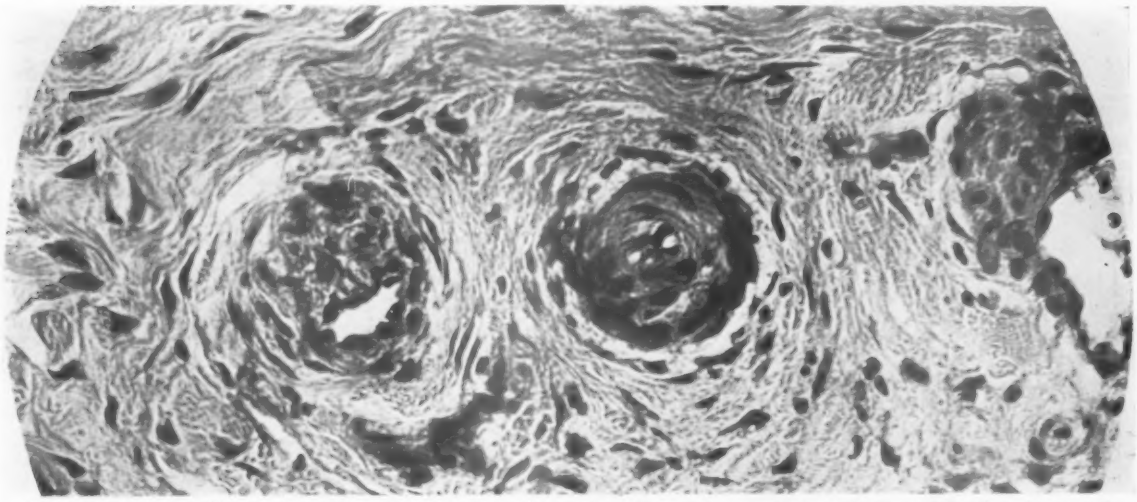

FIG. 6. 9034. Swelling and proliferation of cells of vessel walls, and practical occlusion of lumina in vessels about cervical lymph nodes. Radium, 10,000 mc-hr. thirteen and twelve days before removal. High voltage roentgen rays 80 min., seven and three days before removal.

It seems to be generally agreed that to destroy carcinoma the total dosage must be high but the mode of delivering this dose varies widely. There are three principal methods now widely employed:

(1) The prolonged single exposure to moderate doses of hard rays.

(2) Smaller fractionated doses at varying intervals, usually two or three days, and repeated in series.

(3) The single large and full exposure.

The first is the ideal, selective, non-destructive radiation therapy.

It must be admitted that excellent results have followed each of these methods in a great variety of tumors. The experience and equipment of the operator often limits the choice and too often the vision. The great variety of methods used in uterine cancer with uniformly good results, shows that there at least full dosage is the important essential, the methods of delivering it at least less important. The standardization of methods may however be furthered by considering what particular tissue reactions are found to follow each of the above methods.

(1) The continuous exposure is designed to kill dividing cells, abort the growth and presumably to induce gradual tumor cell atrophy. It is least well designed to call forth defensive tissue reactions, but is doubtless not lacking in such power. It is best calculated to induce growth restraint without damage to normal organs and tissues, and probably should be chosen when growth restraint is the object in view. It is probably the safest, if not the most effective method for many advanced lesions for which palliation rather than clinical cure is all that may be attempted. It is theoretically well adapted to control very sensitive tumors, such as lymphosarcoma and embryonal growths. It is slow, even tedious, comparatively painless, and expensive. That it is effective to a high degree is shown by the results in uterine cancer which are among the best. That it is ideal radiation therapy must be conceded and under suitable conditions its choice must be seriously considered, especially because it is painless. By very similar methods, using roentgen rays, French workers report regression even of laryngeal cancer. The method deserves thorough trial in many situations, especially with bone tumors and deep-seated growths. When growth restraint of resistant or advanced tumors is the object in view, it may be regarded as the ideal theory. It would be interesting to see a series of such cases treated continuously for days or even weeks by continuous mild exposures. Few observers furnish objective data upon which an intelligent choice of method may be based. Nevertheless it would appear that the failure of this technique to excite marked tissue reactions and the uncertainty of its destructive effect on many resistant tumor cells would limit its wide adoption. The proportion of late recurrences after this method is yet to be determined but is probably higher than with more drastic treatment.

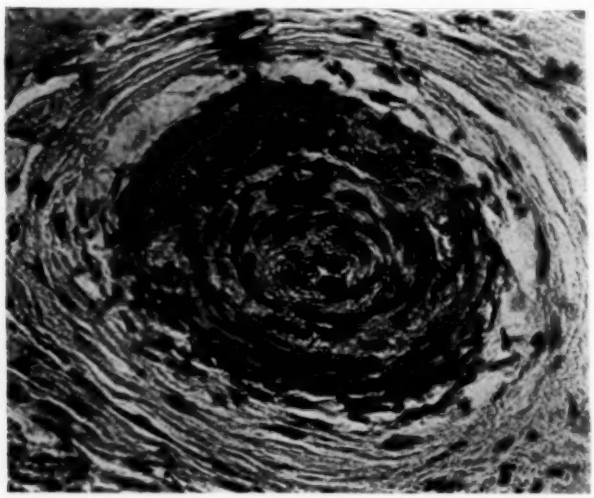

FIG. 7. 7825. Swelling of cells of all coats and occlusion of arteriole in neck after external irradiation; 10,000 mc-hr. radium ten and twelve days before removal.

(2) The method of fractionated dosage has many theoretical advantages and much practical success for its support. On account of convenience and safety, the great mass of radiation therapy follows this plan. Every variety of modification is practiced in regard to time, filtration, voltage, skin distance, intervals and length of treatment, and in general it must be admitted that personal preference and experience rather than established principles, which are lacking, determine the choice. Holfelder recommends small doses over a period of ten days. Wehmers shows that there is increased cell metabolism throughout the latent period so that the second dose acts on sensitized cells, in which finer histological methods always demonstrate changes. Yet under some circumstances previous irradiation may reduce the susceptibility of tumor cells to subsequent irradiation. Russ has shown that grafts made from the Jensen rat sarcoma receiving interstitial irradiation

grow much more slowly than controls and are much more resistant to subsequent irradiation by roentgen rays. Exposure of this tumor to roentgen rays for fifty-six minutes, with a certain set-up, regularly destroyed the growth capacity, but after previous irradiation by radium, an exposure of 90, 135 and even 200 minutes to roentgen rays did not always inhibit growth, although the resulting tumors always grew very slowly, and many grafts failed to grow at all. In the resistant tumors no morphological changes could be observed, except when the exposure was very long. Schwarz advises giving the total dosage on two or three successive days.

The basic principle of this method is the cumulative effect of successive doses delivered upon cells rendered vulnerable by the hyperemia and degeneration excited by previous doses. It may properly rely also upon attacking successive groups of cells during the mitotic period. Again referring to the work of Alberti and Politzer, we find a period of five to nine days following exposure when mitoses are absent and cells more resistant. Human tumors undoubtedly have cycles of growth but that there is any such regular five- to nine-day period of mitotic restoration is certainly not true of the average human cancer. I find mitotic figures present or absent under the greatest variety of dosages and have been quite unable to detect any rule in this matter, except that heavy dosage is required to assure absence of mitoses and that when they have once been eliminated there is a long period before they reappear.

Severe tissue reactions are excited by fractional dosage and they are of the usual type. Reichold reports the disappearance of 5 lip cancers under three successive doses of roentgen rays, 10–20 X, 3 mm. aluminum filter, at intervals of a few days. Section showed at first ten to fifteen mitoses in each square millimeter of tissue. Later no mitoses were seen and cell degeneration became complete. Many vessels with cuboidal endothelium grew into the degenerating tumor. This is a rare and valuable type of report.

Yet when too long continued, or often repeated, it is clear that multiple doses must interfere with the healing process by inhibiting or eventually destroying all the active defense factors which may have been brought into play. Any plan of fractionated dosage must therefore set a definite limit upon itself. Nearly all the cases of abortive fibrosis that I have seen resulted from too great persistence over too long a period with inadequate doses. From the point of view of tissue reactions the operator with fractional dosage should aim to accomplish his object in the shortest time consistent with safety. An exception to this statement may exist when the object is growth restraint.

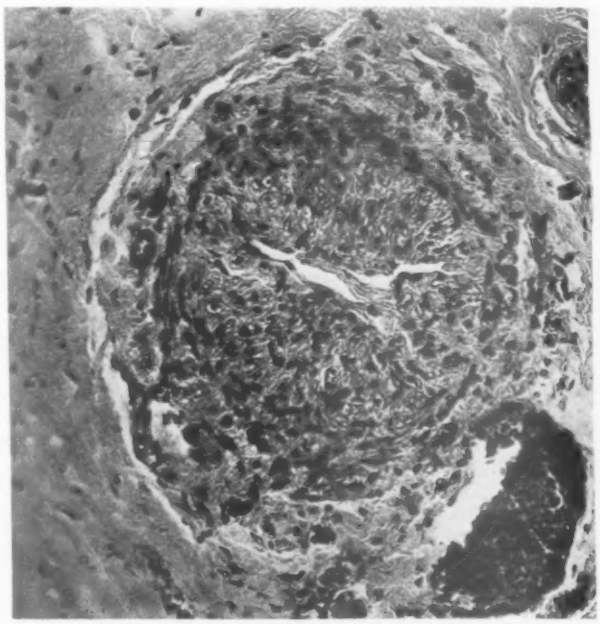

FIG. 8. 9388. Swelling of cells of all coats and infiltration by mononuclear cells of a medium sized artery in neck. High voltage roentgen rays, 80 min., twelve days and nine days before removal.

Béclère, commenting on the bad effects of massive dosage and the good results of small repeated doses in the postoperative irradiation of mammary cancer, offers an explanation which strongly favors the latter method. He refers to the work of Guilleminot, confirmed by Jüngling, on the effects of irradiating seeds (*Vicia faba equina*) in the three states of germination,

hydration, and desiccation. In the three states the radiosensibility is very different. The hydrated grains require six times and the dry grains fourteen times as much radiation to suppress growth as do the germinating grains. These observations establish the law that with divided doses there is always a loss of radiation effect in comparison with a single effective dose.

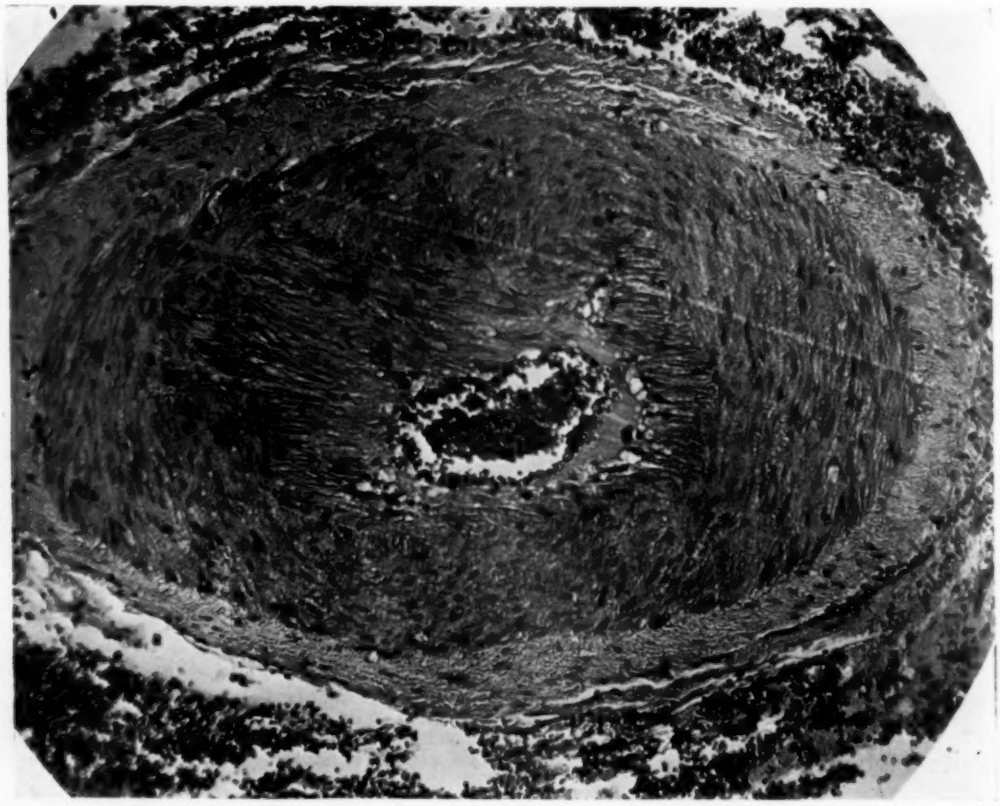

FIG. 9. 9686. Swelling and mucinous degeneration of media of large artery in neck, with narrowing of lumen. High voltage roentgen rays, 80 min., fourteen days and seven days before removal. Radium, 10,000 mc-hr. three days before removal.

But Béclère points out that this law applies only to cells in a state of vital activity, but not to cells in a state of suppressed activity. Guilleminot and Jüngling have both shown that if dry seeds are irradiated the effects are the same whether the total dosage is given at once or is divided. Béclère assumes that the cancer cells remaining after extirpation of the breast are in a relatively latent state and that when irradiated sixteen times during the first year and six or eight the second year they receive a cumulative dosage which the skin would not tolerate in a short period, and are thus destroyed. It may, however, be questioned whether the vagrant cells which cause recurrence of mammary cancer are really latent. They are probably outlying cells from growing edges in infiltrated lymph channels. Yet recurrence may be delayed for several years. I am inclined to suspect that massive irradiation of the operative field in mammary cancer is ineffective because it destroys the natural reparative processes in poorly vascularized fat tissue of skin and axilla. Béclère himself concludes his analysis with the comment that this whole field invites further investigation.

Finding it difficult to sterilize cancerous lymph nodes by ordinary full doses of external irradiation, Quick has shown that

the combination of high voltage roentgen rays (80 min.) and radium packs (10,000 mc-hr.), two of each at weekly intervals, completely destroys certain epidermoid carcinomas in cervical nodes, some of which were distinctly squamous, others of transitional cell type. Very pronounced tissue reactions occurred in the nodes, including extensive plasma cell exudate, and almost sarcoma-like proliferation of connective tissue, while the lymphoid tissue was preserved to a surprising degree. It is evident, from these results that heavy fractional doses thus conducted are capable of yielding quite profound effects on relatively superficial but highly resistant tumor cells, amounting at times to complete sterilization. Theoretically it is perhaps safe to assume that the softer roentgen rays excited most of the connective tissue reaction while the harder radium rays were the more effective in destroying tumor cells. The combined effects of roentgen rays and radium offers an attractive field for research. One often hears that a tumor resistant to one responds to the other agent, but one never hears the explanation. In many other situations the method of large fractional doses over a comparatively short period (4–6 weeks) may be combined to yield results through pronounced tissue reactions, that seem unattainable by other methods. The permanent adoption of this method over a wide field seems assured. Its main hazard lies in the possibility of late undesirable sequelae through the slow progress of arteriosclerosis.

Many clinical illustrations of the efficiency of the fractional plan might be quoted, but they are generally reported without particular reference to the type of tumor, or exact character of tissue reaction excited. Much progress would be attained if observations with this method considered in greater detail the intervals of dosage and the exact type of tumor. We know little about the difference in the effects of doses spaced one week and one month apart, of the relative effects of low or high voltage roentgen rays, and radium rays upon the initial tissue reactions, or about the behavior of different tumors under these successive exposures.

(3) *The single efficient (killing) dosage.* The most impressive results of radiation therapy have undoubtedly been accomplished by the delivery of a single efficient dose at one time. From the point of view of tissue reactions, this method receives the most substantial support. A single intensive exposure devitalizing tumor cells and injuring surrounding tissue sufficiently to cause a severe and adequate reaction is theoretically the best method of irradiating tumors. It is unfortunate that the exact dosage required to accomplish this result has not been determined for the common tumors. At present it must be attempted in rather haphazard fashion, except in the case of interstitial irradiation by radium with which exact dosage has been to a considerable extent standardized.

Intensity of dosage is one of the first essentials of irradiation of carcinoma. However, variation in intensity does not count definitely except between rather wide limits. Matoni has found that when intensity varies between one and four, there is comparatively little difference in action, as judged by the effects on horse beans, but Kronig and Friedrich observed no difference in effects with the same total dosage until the intensity was increased to 1–8. Canti and Spear observed the comparative effects of the same amount of radiation at different distances upon tissue cultures as judged by the influence upon mitoses. When the radium was near the culture, there was no variation in effect by slight differences in intensity, but at greater distances the amount of radiation required to bring about cessation of mitoses was greater than expected from physical laws. Observations on tumors irradiated in the body would probably offer a much more delicate indicator. The intensity must apparently be increased at least five times before notable difference in effects is obtained. Yet, unless radiant energy differs from all other physical agents, its physiological effects must be intensified by the combination of uninterrupted exposure and high intensity. Except for radium needles, I know of few comparative observations on the effects of single continuous full doses. All of these show a high degree of destruction of

tumor cells, marked injury to adjacent tissues, and severe and effective tissue reaction.

The success of this method is attested by a high proportion of permanent cures of favorable cases of resistant cancer, and by many paradoxical results in advanced cases. If exactly the right dosage could be prescribed, more of these paradoxical results would doubtless be obtained. I recall the case of an elderly lady with very extensive rodent ulcer, exposing the bones of face and nose. The late Dr. Janeway, as a desperate effort, applied a very heavy single dose of radium in a broad pack. The patient had a severe local and general reaction, left the hospital and would not return or answer letters, but two years later she appeared in good health without a trace of her extensive disease. Similar results in rectal, mammary and abdominal cancer have occurred too often at the Memorial Hospital, and in the experience of many workers, to be doubted or to be referred to accidental causes. They resulted from a fortunately adjusted large and efficient dosage.

Interstitial irradiation by radium needles represents the best form of single destructive dosage, and this method, in one form or another has established itself as the most efficient in dealing with many localized tumors. There is no longer any interest attaching to reports that radiation cannot control primary localized squamous cell carcinoma in accessible situations. It may not be possible with roentgen rays, but it is possible in a high proportion of cases with interstitial irradiation. There is also little excuse today for the employment of external irradiation for most of these diseases, since it is so often followed by failure and even disaster. The bare glass tubes produce too much necrosis and too much pain, and Failla has replaced them by gold tubes of small caliber. Platinum needles are employed for larger dosage. Such tubes cause severe degeneration and complete sterilization over an area depending upon dosage. One to two cubic centimeters of tissue may thus be sterilized with doses of 2–5 mc. of radium, without much necrosis and with little or no sloughing. The tissue reaction in and about these areas is very severe, including necrosis of tumor cells, leucocytic, lymphocytic and plasma cell exudate and growth of granulation tissue, while over a much greater area there is marked degeneration of tumor cells and all the defensive reactions observed from the heaviest external irradiation.

From a series of experiments conducted at the Memorial Hospital, by Adair, Failla, and Cutler, on the effects of varying the time and quantity of radium buried in the muscular tissue of rabbits, the main results are as follows. Doses of 1–10 mc. of emanation in glass tubes produce about the same amount of necrosis, 6–12 mm. in diameter, and in about the same time (the first few days), after which the dead tissue acts as a filter, but the distant sterilizing effects, with reactive inflammation, increase with the quantity of emanation, and extend over a diameter of one to two centimeters. Large doses, 10–50 mc. in platinum, used for a short time (3–6 hours) fail to cause necrosis, but exert a sterilizing inflammatory reaction over a wider territory, increasing with the dose, and this area may reach two or three centimeters in diameter. With the gold filtered tubes small doses, 1–5 mc., produce very little necrosis, yet some, while the sterilization field is as large as with glass tubes. These results favor the use of varying amounts of radium in gold, brass, or platinum, for short periods where possible, permanently imbedded where necessary. Large amounts of radium, for short periods, may be employed by this method, and since the effects are far more marked than can be obtained by external radiation, this method should probably replace much external radiation and especially deep roentgen-ray therapy.

Against the large single dose externally applied, must be charged many serious disasters, due to overdosage, which assures the patients severe immediate intoxication, a long period of painful reaction, and removes them from the possibility of further treatment for a long time. Interstitial irradiation also is far from ideal, from the patient's standpoint, and because of damage to neighboring structures, especially bone, it may produce painful reactions

which, under many circumstances, must bar the method from consideration. All of these hazards are to be avoided only by great skill and experience of the operator and the exact adjustment of dosage.

DO ROENTGEN RAYS AND RADIUM PRODUCE DIFFERENT TISSUE REACTIONS?

On this matter we have definite information, in some respects, while under others the observations become indecisive. Soft roentgen rays and alpha and beta radium rays produce rapid necrosis of all exposed tissues and show little or no selective action. All soft rays tend to destroy tissues and as sequels lead to long continued imperfect and atypical reparative processes. This well-known principle is illustrated by the clinical history of roentgen-ray burns with their indolent healing and frequent outcome in carcinoma and sarcoma. It is notable that very few carcinomas have followed radium burns which result mainly from repeated exposure to filtered radium. With increasing filtration and higher voltage, the effects of radium and roentgen rays approximate, but it is doubtful if they ever become identical. I have an impression that high voltage roentgen rays are less selective on tumor cells and produce more injury of stroma cells and vessels than do radium packs. We find more mucinous swelling and fragmentation of collagen fibrils and interstitial hemorrhages in breasts and other tissues after roentgen radiation, than after radium packs. There also appears to be more connective tissue produced after roentgen rays than after filtered radium. It appears that sarcoma has never followed exposure in any form to radium. Even in deep therapy my material indicates a preponderance of connective tissue injury and reaction from roentgen rays, and more tumor cell injury by radium. Roentgen rays have not yet reached the hardness upon which selective action appears to depend. If these observations are correct, and some of them date from an early period, then practical use may be made of these different actions. There may be advantage in combining roentgen rays and radium in the treatment of tumors. It may even prove possible to prescribe a combined treatment accurately designed to control the different structural elements in tumors according to their known constitution and to deal more or less separately with susceptible and dividing cells, with resistant and resting cells, with blood vessels, large and small, and finally with the supporting stroma. My colleague, Quick, has already made efforts in this direction.

Several observers have claimed that certain chemical agents are capable of producing much the same tissue reactions, especially in sensitive organs, as radiation. The most important of these studies is that of Werner and others who have adopted the hypothesis that radiation splits lecithin in the cells and produces cholin, and that cholin has a prominent action in inducing the cell changes following irradiation. By injection of cholin, or its combination with boric acid, called enzytol, Werner observed in the lymph nodes, spleen, testis and ovary, changes which he regarded as identical with those following irradiation, especially the nuclear chromatolysis and karyorrhexis. On this basis enzytol has been extensively employed as an adjuvant to radiation. Dorn has given considerable support to Werner's views, but Halberstaedter and Rutten reached contrary conclusions. The use of enzytol has not reached wide adoption, and the observations of Werner seem to indicate merely that cholin is a highly toxic substance for certain cell nuclei. Of such toxic substances there are doubtless many. Thus Dustin finds that hydrochloric acid, trypan blue and trypaflavine produce very much the same nuclear disintegration in the thymus and germinal centers of lymph node and spleen as does radiation. Watjen also observes that in acute arsenical poisoning the lymphoid organs show much the same nuclear changes as after irradiation. All these references may be of interest to those who may be searching for agents to intensify the action of rays.

CONSTITUTIONAL EFFECTS OF IRRADIATION

How much aid can radiation therapy of cancer expect from the body as a whole? It is no longer possible to maintain

that the body furnishes no aid in radiation therapy. There are those who think they observe something akin to a general immunization against the tumor following irradiation, but the grounds for this assumption are inadequately established. None of the known changes in the blood can safely be connected with increased specific tumor resistance. Holthusen suggests that there is a general nonspecific immunization of the body due to protein destruction. The blood coagulability and percentage of globulin are increased after irradiation, which Doerr and Berger attribute to the action of mobilized proteins.

Händel and Tadenuma find that radiation increases the general metabolism of rats, which is reduced by sarcoma, and they conceive that the toxic products discharged by the tumor are at the same time reduced by the radiation. The immediate improvement in health and strength of leucemic subjects following irradiation suggests some such action.

Caspari assumes that the body is immunized by the proteins derived from the necrosing tumor cells, for which he suggests the term necrose-hormones.

A similar view is held by H. Freund, who conceives that there is an immunization process excited by the disintegration products of injured cells, even without the death of the cell. Caspari finds support for his theory in the work of Knipping and Kowitz who find the same increase of fibrinogen and globulin and reduction of albumin in the blood after irradiation as after the injection of alien proteins.

Mahnert's experiments indicate that radiation destroys the glycolytic property of tumor cells and stops the production of lactic acid. Accordingly irradiation is thought to restore the normal carbohydrate balance and conserve the stores of glycogen.

Impressive evidence of the importance of the general reaction of the body, as emphasized by Murphy, and of the local inflammatory defense mechanism in the radiation cure of carcinoma is furnished in the studies of Kok and Vorlaender. Irradiating mouse tumor cells *in vitro* they found it impossible to devitalize the cells by doses of 1500 e (6 epilation doses). By exposing the whole animal to a dose of 10 e (4 per cent of the epilation dose) tumor grafts failed to take. Doses of 225 to 250 e were required to render the tissue refractory to grafts after local irradiation of the tumor bed. Irradiation of the whole animal was somewhat more effective than when the tumor bed was protected. The refractory state from general irradiation appeared at its height in two to five days after irradiation, but gradually disappeared. Regression of established tumors was accomplished by doses of 25 to 50 e. They conclude that while local irradiation was of importance in the results obtained, yet the general reaction was of far greater moment. At times the general irradiation caused the regression of tumors protected from the direct rays. In studying the changes in the regressing tumors Vorlaender emphasizes especially the active and progressive growth of cellular connective tissue and capillaries which infiltrated the tumors and split up the mass into isolated cell groups, in which relation the tumor cells gradually disappeared.

Caspari has confirmed the main conclusions of Kok and Vorlaender. He observed complete healing of mouse carcinoma more uniformly after general irradiation than after single local exposures. Yet the doses required were high (about ½ HED) and often killed the animals. Recurrences were often observed after both methods. Very high doses, 3½ HED, were required to destroy the tumor if given locally, much smaller doses if the whole animal body was exposed. Caspari tries to bring these results in conformity with his theory of immunization by disintegration products of tumor cells.

The significance of all these experiments is somewhat reduced by the fact that the exposures occurred before the implantation or within three days and therefore before the grafts had become firmly established. It may be questioned also whether these results in small animals are applicable to man. A human tumor must itself be irradiated and vigorously, otherwise there are no results. Yet in rare instances very small doses have given very unexpected regressions, which encourages experimentation along this line. The

attempted stimulation of endocrine glands appears to stand without sound theory or tangible result. One may, however, refer to the immunization of animals following the spontaneous absorption of a tumor and trust, without asserting, that similar specific immunization processes may occur in man. At present there is no proof that they do. From clinical observations the impression has often been drawn that the removal of a primary tumor releases growth restraints about metastatic nodules which may appear in explosive form soon after operation. If this is a correct impression, then the irradiation of certain tumors *in situ* is a safer procedure than their removal, especially in advanced cases. At the Memorial Hospital we have an impression that metastases are usually long delayed after irradiation of bone sarcoma, even when the treatment does not prevent the necessity of amputation. All that can be hoped from the body is a vigorous normal reaction to the direct local effect of radiation. That these reactions fail in debilitated subjects has been well shown by Dean who found complete failure of erythema in feeble and anemic subjects, and is proven daily in the experience of radiologists generally. There is no better proof of the essential importance of the tissue reactions in the radiation cure of cancer. In general the radiologist must use every intelligent medical and hygienic measure that may improve the patient's general health, and relieve specific defects from which he may suffer. To treat a cancer patient with radiation alone is highly unintelligent.

Observations are thus slowly accumulating to show that irradiation, in addition to inhibiting or destroying tumor tissue, may exert a favorable influence upon the nutrition and metabolism of the body as a whole, may reduce the deleterious effects of the tumor, and may possibly cause some general nonspecific protein immunization, which increases the resistance of the body against the tumor, and in favorable cases may even throw the balance of nutrition decisively against an unstably nourished neoplasm.

SUMMARY

From this review of some of the tissue changes following irradiation, the following main conclusions may be drawn:

(1) The cure of carcinoma by radiation results from a nice adjustment between injury to tumor cells, assuring their partial or complete necrosis, and injury to surrounding tissues, eliciting a reactive reparative inflammation which removes tumor débris and often destroys viable tumor cells.

(2) These tissue reactions are specific in the sense that taken as a whole they are not observed under any other conditions.

(3) Effective radiation occurs only in tumor tissues which are in an approximately normal state of growth and nutrition and upon tissues which are vascular, well nourished and capable of inflammatory reaction. Dividing cells and rapidly growing tumors are more susceptible than resting cells and stable tumors, but this difference is not invariable.

(4) The three main methods of irradiation, the single, the fractional, and the prolonged dosage, each produces different tissue reactions, and it is desirable that the choice of methods should be determined, as far as possible, by the character of the reaction it is desired to produce, and not merely by the therapeutic effect generally obtained. A high total dosage is the first essential in destroying most true carcinomatous processes, and as a rule the most tumor destruction and tissue reaction, and the best results, are obtained by delivering this dosage as soon as possible.

(5) Radium probably tends to produce more specific selective effect on tumor cells, and roentgen rays more injury and reaction of the connective tissue.

(6) A large part of the destructive effect of rays upon tumors, especially the necrosis of single cells or large masses, in bulky or encapsulated tumors, is caused by interference with the blood and lymph circulation.

(7) Extended observations of the histological changes produced by different doses in the different tumors must be accumulated before radiation therapy can

be taken out of the field of therapeutic empiricism and rendered safe, effective, and uniform. Increased interest and importance thus attaches to the careful and thorough histological study of tumors before and after irradiation.

(8) Effective irradiation excites a favorable reaction on the part of the body as a whole. The nature of this reaction is complex and the factors largely unknown. It is probably of much importance in the cure of malignant tumors by radiation.

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FRACTIONAL ROENTGEN IRRADIATION*

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SOME eighteen months ago, while I was in charge of the roentgen-ray work at the William L. Clark Hospital, a radical change was made in the technique in use prior to that time in the treatment of malignant neoplasms with short wave-length roentgen rays. The time factor of an erythema dose with the apparatus then in use was 90 minutes. The other factors were: 220 kv., 4 ma., 50 cm. distance, filters 0.75 mm. Cu and 1 mm. Al; portals varying in size according to the requirements, and one or more portals as indicated in each case. The time factor then in use varied from one-half to one erythema dose per portal, and treatments were repeated in from four to six weeks.

While the results with this technique were often very satisfactory, there were a number of recognized objections: (1) the danger of an overdose. With a full erythema dose any idiosyncrasy of the patient, or carelessness in the technique (such as the omission of the filter), was a matter of very grave danger; (2) there was always fatigue and discomfort associated with the prolonged treatments; (3) considerable systemic shock frequently followed; (4) in many cases roentgen sickness occurred with resulting exhaustion, and (5) there were the permanent pathological changes which were often

* Read at the Twenty-sixth Annual Meeting, American Roentgen Ray Society, Washington, D. C., Sept. 22–25, 1925.

produced in the healthy tissues in the neighborhood of the neoplasm.

In searching for a means by which to reduce, at least, these objections it became evident that the time factor was the only one which could be altered without eliminating some of the essential characteristics of the other factors. Thus, to have reduced the voltage or the milliamperage would have reduced the total intensity of the roentgen-ray beam without commensurate benefit, and to have increased the filtration would have likewise reduced the intensity without rendering the beam more homogeneous.

For several years past radiologists in America have been gradually abandoning the "lethal dose" technique, as it has come to be recognized that it is quite impossible to kill all the cancer cells in a tumor by even the heaviest doses. Though a heavy dose may be fatal to more tumor cells than a light one the damage done to the surrounding normal cells is such as to produce permanent pathological changes which not only interfere with the normal functions of the cells but also inhibit a healthy reaction against the invading cancer cells.

It is of course realized that the first essential in any form of therapy is that the general resistance of the body must not be undermined. What is required, therefore, in radiation therapy is a dosage which will impair the vitality of the malignant cells and will, at the same time, stimulate the surrounding normal cells. This should be possible as it is known that malignant cells are more sensitive to radiation than are most of the normal body cells. With this in mind, therefore, some radiologists have reduced their dosage to one-half, or even to two-thirds of an erythema dose per portal, and repeat their doses a little more frequently than before. Undoubtedly the fear of stimulating the malignant cells to greater activity by really small doses, as was suggested by the Arndt-Schultz law, has deterred radiologists from using them. There is no proof, however, that any such stimulation does occur. We do not yet definitely know the factors which cause certain cells to become malignant, nor do we know exactly the biological effect of the rays on either malignant or healthy tissue. We do know, however, (to quote Hirsch[1]) "that there is a differential action of the rays on cells in various stages of health and disease, youth and age. A small dose may do much harm to a group of cells in one condition and leave another group comparatively untouched to grow and proliferate. A large dose, on the other hand, would do more general harm and affect cells of varied groups and so impair the general vitality of the growth and of the surrounding tissues. It is a fallacy to believe that the radiation cures cancer by destroying the cancer cells. To do so is not to take into consideration the reaction of the living tissue in the restoration or acquisition of immunization power nor consider the local reparative process which plays the main rôle in the healing of the tumor . . . Optimum reaction of the immediately adjacent tissue which plays so important a part in the production of the clinical cure is attained by small and moderate doses, but is prevented by larger ones."

In the early days of roentgen therapy small, frequently repeated doses were used in the treatment of superficial lesions because, having no method for measuring the output of the tube it was considered dangerous to give large doses at one sitting. Although there was considerable difference of opinion as to the relative value of low and high vacuum tubes, target skin distance, length of exposure, etc., the reported end results of most of the workers appeared to be excellent. To quote Martin,[2] "The most popular technique at that time required an exposure of ten minutes to the unfiltered rays of a low vacuum tube at a target-skin distance of from six to eight inches, with a parallel spark-gap of about three inches . . . When the hot wire milliammeter reached a point in its development where it was, in a measure, reliable we learned that we had been using a high voltage current of approximately two milliamperes . . . Unfiltered doses of twenty milliampere-minutes administered at a target-skin distance of twelve inches with a three inch spark gap would

[1] Hirsch, I. S. The Principles and Practice of Roentgen Therapy. American X-Ray Publishing Co., New York, 1925.

[2] Martin, J. M. Fifteen years' experience with fractional dose method of treating cutaneous malignancies. Am. J. Roentgenol. & Rad. Therapy, 1923, x, 726–733.

produce a tanning of the skin when repeated three times within a period of ten to twelve days."

Roentgen rays so produced consisted largely of the longer wave lengths and were nearly all absorbed by the superficial layers of tissue, nor were there any (practically speaking) of those short wave length radiations which, both directly, and through scattered radiations, we now know to be essential in the treatment of deeply lying neoplasms. In treating such cases the effective wave length of the beam utilized must be very short, which means that the tube must be operated on much higher voltage than was possible in the early days of roentgen therapy. The total intensity of the beam is, likewise, at the present time, so greatly increased that we can afford to cut out the soft components by using heavy filtration, still retaining sufficient of penetrating radiations for practical results. This tends not only to protect the overlying tissues from serious injury, but it also has the advantage of rendering homogeneous that portion of the beam which is not absorbed by the filter, a condition which, according to Dessauer, is essential to proper deep therapy. By the use of this high voltage, and of homogeneous radiations, the percentage of the surface intensity which exists at any given depth is increased.

Some years ago tables were published in which the intensity at various depths of tissue was given as a result of calculations based on the half-absorption value of tissue and the law of the inverse square, but without any consideration of the effect of scattered radiation. A part of the roentgen-ray energy is directly absorbed in passing through matter and part is absorbed through scattering. The amount of total absorption is dependent on the density of the absorbing substance and the wave length of the roentgen rays. "With hard rays the scattering makes the major contribution to the total absorption, whereas with soft rays the true absorption plays the predominating part, particularly in elements of low atomic weight . . . The true absorption may become less than the scattering so that the latter becomes the primary factor in determining the total absorption. This is particularly true of the substances composed of elements of low atomic weight, for example, air, water, and tissue. These substances scatter more than they absorb. It is believed that from forty to fifty per cent of the biological effectiveness of highly penetrating rays is due to scattered rays" (Hirsch). Therefore, the tables, to which reference was made a few moments ago, are perfectly useless because no account is taken of these rays. Nor does it appear any more logical to criticize fractional doses under modern conditions, as has been done, because some years ago the treatment of deep-seated neoplasms, with the radiations then available, did not prove successful.

Many observers now believe that a direct destruction of the malignant cells, *per se*, is not essential to their ultimate disappearance. Two theories are advanced to account for the disappearance of malignant tissue under radiation. The first is that the action is a direct one on the tumor cells. The second, that it is due to the proliferation of connective tissue cells which replace such tumor cells as are destroyed, and so split up the remaining viable cells into harmless groups, temporarily so at least. Undoubtedly both of these changes play an important part in the healing process. Retrogression of a cancer may not be entirely caused by the local action of the rays, but may also indicate a reaction of the surrounding normal cells against the cancer attack. Invasion of the tissues by any foreign cell generally produces some form of cell reaction, indicating an attempt of the body to mobilize whatever forces are at its disposal to combat the invading cell. It seems reasonable to suppose that the metastatic and undifferentiated cell, behaving as a foreign substance will call out a similar body reaction (Asnis). The preservation of vital tissue in the periphery of the tumor, therefore, becomes a matter of prime importance. That the normal cells do play an important part in the destruction of cancer cells, even in unirradiated cases, is evidenced by the presence, in the few such cases which have been reported, of lymphocytic infiltration, degenerated cancer cells, fibrosis and hyalinization. Following local

irradiation certain specific substances of the nature of antibodies have been observed in the blood. Heavy dosage is unfavorable to the formation of such antibodies and, in addition, has a deleterious effect on the bone marrow, spleen, lymphatics, liver and suprarenals. In this way a condition of roentgen-ray cachexia is brought about; both local and general resistance is reduced, and reparative processes inhibited.

When heavy radiation treatment came into use the "cross fire" technique was introduced in order to spread the effects over as much skin surface as possible while concentrating the rays at a focus in the deeply lying tumor. Small portals of entry were essential in most cases in order to reduce the danger of the overlapping of exposed skin areas while attempting to give the maximum dose to the tumor. However, as scattered radiation is responsible for a large fraction of the total depth dose, it must not be forgotten that the magnitude of the dose at any depth depends on the size of the cone of rays used. Kroenig and Friedrich, for example, have shown that with a portal of entry of 12 cm. × 12 cm. the dose at a depth of 8 centimeters in water is almost twice that obtained at the same depth with a portal of 4 cm. × 4 cm. Again, Handley points out: "In every carcinoma there is a comparatively small number of perfectly healthy and active cancer cells, with a large mass of more or less degenerated and dying cells. The former class of cell is to be found in the peripheral lymphatics of the microscopic growing edge and at the edge of the microscopic nodules of growth which are still in the active infiltrating stage." According to this view of the method of growth and invasion of the tumor the radiation should be applied to a large area outside of the main tumor mass. The difficulties of so doing are greatly increased by the use of small portals of entry.

Finally, several methods have been devised with a view to the accurate directing of the radiation through several portals. It is, of course, first necessary to determine the relative position of the lesion in relation to certain fixed points, and secondly, the depth from the surface of the body. These data are obtained by direct measurements, by indirect measurements through roentgen examinations, by the use of calipers, flexible lead strips, etc. But with all these it is questionable as to how close we come to judging either the correct size or position of an invisible lesion, and certainly we obtain very little or no indication as to the extent of the microscopic involvement of the neighboring tissues, which is a point of the greatest importance. Even if our localization is perfect, the final "cross firing" of the beam still remains largely a matter of guesswork.

It was in consideration, therefore, of these various points that the change in the technique was made. The kilovolts, milliamperes, distance, and the filters remained the same, but I began using the full size of the treatment cone (about 200 sq. cm.) in every case, and reduced the time factor very considerably, repeating the dose at frequent intervals for comparatively long periods. Cases where the malignant mass lies within 5 centimeters of the surface I treat with doses of from 3 to 5 minutes twice daily, for from one to two weeks. After an interval of two weeks a second, and later a third, and even a fourth, series is given. When circumstances render it impossible for the patient to report twice a day the dose is reduced to one treatment which is sometimes extended by the addition of a minute or two. Similarly for lesions lying deeper than 5 centimeters the time of exposure is increased, and 5 or 10 minutes are given twice daily over similar periods. No attempt is made to prevent overlapping of the portals of entry, but cross fire irradiations are used in order to reach the tumor from all sides and thus to obtain as uniform a radiation as possible. By this technique there would seem to be less likelihood of outlying metastatic nodules escaping treatment.

Other advantages of this technique I have found to be as follows: The dangers of an overdose are enormously reduced; the fatigue of the long treatments is eliminated; there is no systemic shock; radiation sickness is very rare; and the

normal surrounding cells are not injured. In addition to the morphological changes which occur in many of the malignant cells (vacuolation, karyolysis, and ultimate necrosis) there is an active round cell infiltration which replaces the destroyed cancer cells. Subsequently this is changed into sclerotic connective tissue. If large doses of radiation are given to the tissues with the object of killing all the malignant cells, the effect is to produce a surrounding zone of necrotic tissue where healthy tissue should be, and this acts as a barrier against regenerative processes. It has been observed, also, that when normal structures, such, for example, as the parotid gland, are unavoidably exposed to these small doses, the resulting loss of function is only temporary, thus demonstrating that the normal cells are not permanently damaged as would be the case with heavy doses.

It is surprising how soon after beginning treatment the beneficial effects of the small doses become evident. First to be noticed by the patient, generally within two or three days, is a general feeling of well-being. Then, in most cases the pain, when present, is greatly relieved. This has been particularly noticed in cases which have previously received heavy doses without apparent benefit. It has, indeed, been a most striking feature in several cases. A diminution in size and induration of the tumor is frequently noticed long before what is generally considered a "lethal dose" has been given. In an encouraging number of cases this beneficial effect has been continuous although the time has not yet been sufficient to draw final conclusions. In some others the cells have seemed to acquire a resisting quality. As was to be expected a "cure-all" dosage has not yet been found.

Although some of these treatments have extended over long periods I have not yet seen a typical erythema as a result. The skin early shows a tanning which in some cases becomes very marked. So far, however, the skin changes have gone no further and in the short intervals between the various series of treatments much of the tanning disappears. Whether there will be a late appearance of those roentgen-ray skin lesions which have sometimes occurred in the past, following prolonged irradiation, remains to be seen. It is my belief, however, and certainly my sincere hope, that they will be avoided by the use of the highly pentrating, heavily filtered, rays. Before closing I should like to illustrate what may be accomplished with these small doses by reference to 3 of the cases which I treated by this technique while at the William L. Clark Hospital.

CASE REPORTS

CASE 1. Carcinoma of the tongue and floor of the mouth. This man noticed some induration under the right side of his tongue in 1922. He consulted a physician, in 1924, who diagnosed the condition as carcinoma. A piece of the tissue was examined microscopically at George Washington University and the diagnosis confirmed. While in Washington, needles containing 25 mg. of radium element were implanted on July 25, 26, and 28, and were left in place for four hours on each of these days. As a result a large slough occurred, and there was much and continued pain. In the latter part of August roentgen-ray treatments were given (factors, 175 ma-min. 9 in. spark gap, 14 in. dist., filter 0.026 mm. Cu + 1 mm. Al., 4 doses).

Two "stumps" of the growth still remained, and at the end of September two more 5-hour treatments with the radium needles were given. The pain steadily increased. He was then taken by friends to the Howard Kelly Hospital, in Baltimore, where it was decided not to give any further radiation treatment, and he was referred to the William L. Clark Hospital, in Philadelphia, for electrocoagulation. As Dr. [illegible] was away the case came directly under my care. When I first saw him he was suffering intense pain. His features were drawn and haggard. He had been losing weight rapidly, and sleep was impossible. His breath was foul smelling as there was considerable slough still present under the right side of this tongue. He had absorbent cotton stuffed between his teeth and his tongue, as contact caused him such acute agony. His tongue and the floor of his mouth were much swollen and indurated, some of this being, no doubt, of an inflammatory nature. His condition altogether appeared to be hopeless.

After examination I decided that the case was not one for coagulation treatment and telephoned to Dr. Kelly that I proposed giving fractional roentgen irradiation, to which he

agreed. Treatments were begun on December 10, 1924. He was given 5 minutes twice daily to each side of his neck through large portals. Twelve such treatments were given in succession. There was then an interval of twelve days, after which he received 3-minute treatments twice daily for five days. Quite marked edema occurred at this time so that treatments were suspended for nearly a month. The pain had diminished considerably although it was still necessary to continue the use of hypodermics of morphine at night.

Beginning February 9, he received treatment for ten days more, 3 minutes, twice daily, over both sides of the neck and face. He was then so greatly improved that he was able to return home. He no longer required hypodermics, but took some sedative pills with him for use at night. With the help of a little will power, however, he found he was able to do without even these. He remained away for six weeks and then returned for another series of treatments. These consisted of similar doses, for a period of eleven days. He then again returned home and to work which he has been able to keep up ever since, reporting to the hospital from time to time for observation. On one of these occasions I found what looked like a small papilloma springing from the area from which the radium slough had come. However, no malignant cells could be found on microscopic examination.

In all, this patient received seventy-four fractional roentgen-ray treatments over each side of the neck. At one period he complained bitterly of the dryness of his mouth, but for some months past he has not been further troubled in this way. His present condition appears to be very satisfactory.

The interesting feature about this patient is the remarkable way in which he improved under the small doses although his condition was steadily growing worse under heavy irradiation. It has been suggested that the heavy doses were really what brought about the improvement but that their effects were delayed. It is, of course, impossible to prove the contrary, but to those who followed the case through there seems no possible doubt that the whole aspect of the case changed very soon after the small doses were begun. Similar results in several other cases of a like nature have confirmed me in this belief.

However, to show what can occur in malignant conditions where no previous irradiation has been given the following case is presented:

Case II. Recurrent carcinoma of the breast following amputation. Dr. Harvey Righter, of Philadelphia, performed the operation. The patient refused radiation treatment, and was warned to report for frequent inspections. She did not return, however, till four years later, when she had considerable ulceration along the line of the old incision in the left breast. There were large indurated glands in both supraclavicular areas. The right breast was large, much indurated, and wholly adherent to the chest wall. There was, also, a large ulcerated area around the nipple. Her general condition was fairly good. Treatments were begun on July 14, 1924. She received 8 minutes' treatment daily, through large portals, over the supraclavicular area, the breast, the axilla, and the scapula, of each side, for five days. Treatments then had to be suspended as she was obliged to leave the city, but were resumed, on August 5, when she returned. She was then given 10 minutes' treatment daily, anteriorly, over each supraclavicular region, each breast, and, laterally, into each axilla. There followed an interval of three weeks, when another similar series was given during the following nine days. There was again an interval of two weeks, followed by seven days' more treatment. At that time the ulcers on both breasts had entirely cleared up, the indurations in the supraclavicular areas had disappeared and the right breast had become perfectly soft with the exception of an area in the center the size of an egg. The breast was also quite movable on the chest wall. The patient felt a great general improvement. No more treatments were given for five months at which time the lump in the right breast had become still smaller. Ten days' more treatment were then given, of 5 minutes, over the same areas as before. Ten weeks later she was given six days' similar treatment.

I saw this patient a few days ago with Dr. Righter. She had just returned from a long automobile trip, and reported that she felt in splendid condition. The indurated area in the right breast had diminished in size and felt like a flattened plaque of scar tissue.

These two cases illustrate what can be accomplished with superficial lesions. In the next, the lesion was deeply seated.

Case III. Carcinoma of the uterus with diffuse abdominal metastasis in a young woman of twenty-five years of age, the mother

of five children. She was sent to the Wm. L. Clark Hospital after Dr. John Deaver had performed a laparotomy and found further operation to be impossible on account of the extent of the involvement. When I first saw her she had lost a great deal of weight, she was unable to eat, and vomited very frequently. Her color was pasty, and she had a very haggard expression. There was considerable ascites. Multiple indurated tumors could be felt both on superficial and deep palpation of the abdomen. Her condition appeared to be desperate.

Treatments were begun on January 26, 1925, and consisted of 10 minute exposures, daily, for eleven days, over the right and left sides of the pelvis and abdomen. Large portals were, of course, used. After a two weeks' interval she had similar treatments for the next twelve days. At this time she already showed considerable improvement. She seldom vomited, and she had begun to do work about the house which she had been quite unable to do for many months previously. Her abdomen was tapped and considerable fluid withdrawn. After a rest of two weeks she was given treatments for nine days. Another rest of three weeks was followed by treatment for eleven days more. By this time she was putting on weight, and her color was greatly improved. Her general condition was much better. The abdominal tumors were fewer and very noticeably smaller. She was again tapped and a smaller quantity of fluid obtained than on the first occasion. She received treatment for five more days in June. I saw this patient, also, a few days ago. She is now able regularly to attend to her housework and her five children. She is slowly gaining in weight. She no longer suffers from constipation. A little fluid still collects in the abdominal cavity, but not nearly so much within the past several months as in the preceding month.

It is fully realized that perfection has not yet been attained in the treatment of malignant neoplasms by roentgen rays, but if such encouraging results can be obtained by the use of small fractional doses, are we justified in exposing our patients to the dangers and discomforts (both immediate and remote) of the longer treatments at present more generally in use?

DISCUSSION

Dr. Robert E. Fricke, Baltimore. Dr. Morgan has presented a new concept of roentgen-ray therapy which shows great promise and merits conscientious trial.

To date we have not employed the fractional method in apparently curable malignancies, for two reasons. In the first place our experience with radium at the Howard A. Kelly Hospital has indicated that our best chance to cure is by the initial massive dose. If this does not exterminate the growth, cure is still possible but the prognosis is distinctly less favorable. Secondly, our roentgen-ray therapy at present is conducted with a high voltage, high intensity water-cooled machine, which with heavily filtered rays gives a light erythema dose in seven to ten minutes. This shortening of the time factor obviates several of the disadvantages quoted in connection with massive dose roentgen irradiation; namely, the fatigue and discomfort associated with prolonged treatments, the systemic shock, and the radiation sickness with resulting exhaustion. We guard against omission of filters by using permanently fixed plates.

In advanced, hopeless, malignant conditions, where palliation and prolongation of life is the main object, we have a vastly different proposition. Here we have had a good deal of experience with fractional roentgen irradiation, and the result has been almost uniformly gratifying. The outcome has been frequently far beyond our expectations. I will cite some recent cases.

A patient from Harrisonburg, Va., aged sixty, suffered since the Spring of 1923 with epigastric pain and vomiting. May 26, 1924 Dr. George G. Snarr of Winchester, Va. operated and found a massive carcinoma of the stomach with some glandular involvement, and performed a posterior gastroenterostomy. Dr. Hodges of Richmond, Va., gave roentgen treatments in the Summer of 1924. From September, 1924 the patient suffered a great deal of abdominal pain and lost much weight. Dr. Hawthorne of Winchester, Va. referred him to us March 11, 1925. Dr. Kelly examined and found a fixed nodular epigastric mass measuring 10 cm. horizontally by 6 cm. vertically. I gave three series of fractional roentgen-ray treatments, in March, in May, and from August 31 to September 18, 1925. The factors were 240 kv., 40 ma., 50 cm. distance, filtration 1 mm. copper and 1 mm. aluminum, large portals over the epigastrium and left lateral abdomen, one or two minutes every two days. This patient has kept up his weight, his blood count is good, the pain has disappeared and vomiting has ceased. He complains only of spells of extreme weakness. The abdominal mass gradually diminished, until on examination September 16, Dr. Kelly could find no disease palpable in the abdomen.

This case stands in marked contrast to that of a patient to whom I gave a massive roentgen-ray exposure over the epigastrium in November, 1923. She vomited all food for two weeks following this treatment and passed away ten months later.

Another patient had an advanced squamous cell carcinoma of the floor of the mouth. November 24, 1924 radium treatment was given; December 3, 1924 Dr. Kelly used electrocoagulation on the growth in the floor of the mouth and in a metastatic gland in the right side of the neck. January 15, 1925 heavy implantation of radium was carried out. In March, 1925, the patient was confined to a hospital with excruciating pain, almost comatose, able to eat very little. During April 1 gave a series of nine fractional roentgen-ray doses, 2 minutes a day, through the right cheek, resulting in gradual complete disappearance of the pain. When last examined, August 21, 1925, there was some induration in the floor of the mouth, probably scar tissue; the bone was exposed; there was no obvious growth, no glands in the neck, and no pain, as a result of the combined effects of radium, coagulation, and the roentgen ray.

In conclusion, from our past good results we expect to continue fractional roentgen radiation in extensive malignancies of the upper abdomen and of the mouth and throat; also in Hodgkin's disease, where for some unknown reason massive treatment seems to induce severe systemic shock and radiation sickness.

ANEURYSMS OF THE INTERNAL CAROTID ARTERY AND THE CIRCLE OF WILLIS, FROM A ROENTGENOLOGICAL VIEWPOINT

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THE purpose of this paper is to bring before roentgenologists the incidence, etiology, symptomatology and especially the roentgenographic appearance of aneurysms of the internal carotid artery and the adjacent arteries of the circle of Willis. We intend to show that it is quite possible to make an accurate ante mortem diagnosis in a certain percentage of these cases, and that a careful study of skull films in these cases may clinch the diagnosis for the clinician. This is in contrast with the views held by Beadles[3] who, in 1907, basing his comments on the study of 555 cases of intracranial aneurysms which were found at post mortem, concluded that, "It is quite impossible to diagnose an aneurysm of any one of the cerebral arteries except in the most unusual circumstances." Later observers, notably Cushing[13] and Symonds[12] have been more optimistic, and have even made the diagnosis in a small number of cases. Little attention, however, has been paid to the appearance of these aneurysms as revealed by the roentgen ray.

Schüller[10] in his excellent monograph on cerebral roentgenography mentions that calcification may be seen in the wall of an aneurysm or cyst, and reports one case in which an aneurysm found at autopsy was roentgenographed and calcium plaques demonstrated. The head had not been examined before death. He fails to specify anything characteristic in appearance, location or clinical findings which would differentiate between aneurysm and cyst.

Heuer and Dandy[7] record the most striking case we have seen, one of large bilateral aneurysms with many typical areas of calcification, but they failed to recognize it as such until autopsy revealed its nature.

Stewart[11] states that, "Radiography is of particular value in the diagnosis of aneurysms of the cranium, chest and abdomen," but fails to give any details or descriptions in the intracranial group.

Locke[14] reports the roentgenographic findings in his cases but they are arteriovenous aneurysms and such are not included in this report.

Cushing and Symonds fail to mention the value of films except in one case where it is reported that "*x*-ray was negative."

Kirby,[15] however, in reporting a case, states that "*x*-ray examination showed a mass in the right middle cranial fossa eroding the sella and the floor of the middle fossa," but again it was not recognized as an aneurysm.

The first case diagnosed as an aneurysm by means of the roentgen ray, as far as we have found, is that one reported by Spiess and Pfeiffer,[18] an extradural aneurysm of the internal carotid artery "as large as a child's fist," visualized because of calcium in the wall. This was confirmed by autopsy. This case was also quoted by Schüller in 1924.

INCIDENCE

It is remarkable that not more has been written regarding the possibilities of roentgenological recognition of this condition when we consider the large number of cases which have been reported. Fearnsides[6] in his excellent review of this subject says "the presence of a saccular aneurysm of one of the basal cerebral arteries at necropsy is one of the commonest of pathological findings." He gives Biumi, of Milan, credit for reporting the first case of this kind in the literature (1765). In 5,432 post mortems at the Pathological Institute of the London Hospital (1907 to 1913) 51 cerebral aneurysms in 44 necropsies were discovered. Twenty-six of these occurred on the carotids or their immediate branches. Osler[4] in his first 800 post mortems at the Montreal General Hospital found 12 aneurysms of the basal arteries of the brain. Lebert[1] collected records of 86 cases. He found that 47 of these arose from the carotids or the larger arteries immediately adjacent. The left internal carotid was affected more often than the right in his cases. Von Hofmann[2] published an account of 78 cases. The order of frequency of the various arteries involved was, (1) middle cerebral; (2) internal carotid; (3) anterior communicating; (4) basilar; (5) vertebral, and (6) anterior cerebral. Beadles[3] collected the post mortem reports of 555 intracranial aneurysms, 114 of which represented new material. Locke,[14] assembled reports of 588 cases of pulsating exophthalmos with post mortem findings in 50 of them. Thirty-two of these showed communications between the internal carotid and the cavernous sinus, 7 showed tumors, 4 had aneurysms of the carotid, 3 revealed aneurysms of the ophthalmic artery and in 4 no lesions were found. Twenty-five of the 121 cases he reports were roentgenographed. Of these, 13 were reported as negative, 5 showed foreign bodies (war wounds), 4 showed fracture, 2 revealed thinning or erosion of bone and one suggested tumor.

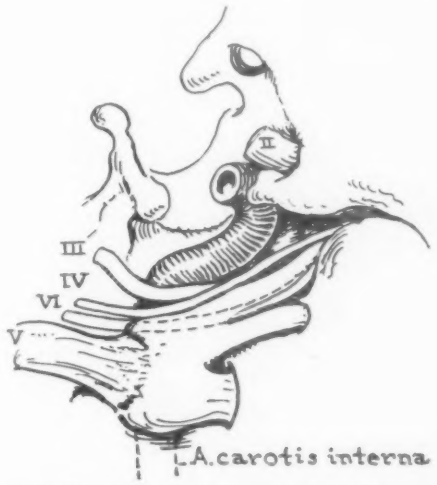

FIG. 1. A diagrammatic representation of the relation of the intracranial portion of the internal carotid artery to the sella and to the second, third, fourth fifth and sixth cranial nerves (seen from above and from the side).

Wichern[5] published the clinical histories and post mortem findings of 22 new cases, and concluded that aneurysms of the cerebral arteries are not rare but that the infrequency of diagnosis is due to the fact that they are rarely considered.

In Cushing's clinic there have been 4 cases of aneurysm of the arteries at the base of the brain found or verified at autopsy in 284 post mortem examinations of the brain. Two other cases have been recognized at operation, in something

over 1200 cases of proven intracranial lesions. At the same time the medical service has had 4 cases revealed at autopsy out of 904 post mortems, in 297 of which the brain was examined. There is in addition another group of cases which are classed as "brain tumor suspects" in whom the nature or character of the disease has not been proven, this group being probably half as large as the other. There are certain of these which are probably aneurysms of the carotid, as will be shown below.

PATHOGENESIS

Our group of cases is too small to permit of any extensive pathological or etiological study and deductions, in face of the widely divergent opinions which have been expressed in the literature. Five main factors are considered, and various authors place the emphasis on different ones. From a summary of the literature and our own experience, the causative factors are grouped as follows: (1) Degenerative or arteriosclerotic weakening of the arterial wall; (2) those due to infected emboli, usually endocarditic in origin; (3) trauma to the artery; (4) syphilis, and (5) those of unexplained origin which are classed as "congenital."

(1) The most common type is the one due to degenerative changes in the media of the artery, allowing saccular dilatations or outpocketing. These are apt to be large aneurysms, frequently single, are of long duration with a history of many or repeated "attacks," and are the ones most apt to be recognized by roentgen examination, due to the associated arteriosclerosis and calcium deposits, with resultant direct visualization on the films, or to their long-continued expansile pulsations with erosion of the neighboring bone. This type of aneurysm naturally occurs in persons of advanced years and is well illustrated by Case B-4. These aneurysms are most commonly located on arteries of the first order, and are frequently found at the point of bifurcation or branching, so that it is difficult and sometimes impossible to determine the exact point of origin.

(2) A fair percentage of all cases reported are associated with endocarditis, and a study of the aneurysms in these cases may show acute changes, sometimes with demonstrable infection. These are presumably embolic in origin, are of sudden onset, short duration and occur, for the most part, in young people. Other infections may play the etiological rôle but they are rare.

(3) Trauma is only occasionally a causative agent, as is presumably the case in the report by Kirby[15] in which the films showed an old fracture through the base of the skull. The aneurysm, as revealed at post mortem, measured 4×5 cm. No statement was made as to the presence of calcium deposits in the wall of the sac. The factor here is evidently a tear in the arterial wall, due to a foreign body, a missile, or a fracture of the subjacent bone. The rupture of the wall is apparently incomplete, but allows an extravasation of blood which is walled off by the adventitia or even by the surrounding structures. If recovery from the initial violence occurs, there is apt to be organization of the clot, sometimes with deposition of calcium, again allowing direct visualization on the films. The signs and symptoms in this type of case begin with the trauma and either remain stationary or gradually decrease coincident with absorption of the clot. A more common sequel of trauma is the formation of arteriovenous aneurysms which give a fairly definite clinical syndrome as reported by Locke.[14] Two of his cases are from this clinic, but are not included in this report.

(4) Contrary to the findings in aneurysms of arteries elsewhere in the body, syphilis as an etiological factor is rare. In our series only one case had serological or clinical evidence of syphilis. Other writers, since the use of the Wassermann test has become general, report the same findings, and it is estimated that not more than 5 per cent of intracranial aneurysms are due to, or associated with, syphilitic involvement.

(5) There remains a fair-sized group of cases, many of them in young people, in whom no concomitant or antecedent disease can be found, and in whom there is

no evidence of trauma or of arteriosclerotic degeneration. Histological study of the aneurysms in these cases also fails to reveal any etiological factor or any known pathological process. This group is therefore classed as congenital for want of a better name. The history and findings in this group of cases are apt to be variable and atypical, and the aneurysms usually small.*

SYMPTOMATOLOGY

The most constant physical signs and symptoms and those of the most diagnostic value are the ones due to the aneurysm itself, especially the rupture thereof. Next in value are the "neighborhood" signs due to pressure upon the adjacent structures. These signs may be simulated by any other disease or tumor which happens to occur in the same location. Symonds[12] adds a third group, those due to the disease causing the aneurysm, but these are inconstant and unreliable. The roentgen findings will be discussed separately.

1. A *sudden* onset of symptoms is usual, which is due to the rupture of the aneurysm or a leakage of blood through a weakened portion of its wall. Prodromal headaches may be present, which are apt to be throbbing or pulsating in character on careful analysis. If present, there is to be expected a sudden exacerbation followed by gradual clearing up of the signs of pressure, which may be more quickly relieved by lumbar puncture as in Case A-5. With the exception of the fatal cases, the recovery from an attack is more rapid than in intracerebral hemorrhage, and the signs of meningeal irritation may be more marked. Wichern,[5] and Symonds[12] suggest that these two points may be important in differential diagnosis. With the suddenness of the onset *coma* is noted, occurring in 60 per cent of our cases. This may be transitory or prolonged, probably depending upon the amount of extravasation. Subsequent attacks of varying severity may occur, due to repeated leaking of blood from the aneurysmal sac. Death, of course, may follow any one attack and in 2 of the 8 autopsies only a single attack was noted, ending fatally.

Lumbar puncture should yield a homogeneously bloody fluid, if performed at or shortly after the sudden onset or exacerbation. If the puncture is done between attacks the fluid may be xanthrochromic. In our cases this was noted once twenty-one days after an acute onset (Case B-6) and once twenty-four days after an acute exacerbation of symptoms (Case B-5). It is possible that there was a slow leak or a gradual closing of the ruptured point as blood ordinarily disappears quickly from the spinal fluid.

Pain is usually present, as distinguished from headache, and is commonly unilateral, sometimes referred to the neck and shoulder, or to the trigeminal area, especially the upper division. The pain in the neck may be associated with stiffness and may erroneously suggest a meningitis. This feature was marked in Case A-8 and led to antimeningococcus therapy.

Hemorrhages beneath the retina (subhyaloid) as reported in Case B-2 may be important in directing the finger of suspicion at the internal carotid. Hemorrhages *in* the retinae are seen more frequently but are of less value in differential diagnosis, as similar areas may be found in injuries, local disease of the vessels, cardiac disease, embolism and thrombosis, nephritis, pernicious anemia, leucemia, hemophilia, purpura, scurvy, septicemia, diabetes, malaria, phosphorus poisoning, etc. The direct extension of the hemorrhage within the sheath of the optic nerve was marked in Case A-3 and also present to a lesser degree in Case A-4.

2. The neighborhood signs and symptoms are those of pressure, usually involving the third, fourth, fifth and sixth nerves, less frequently the second and seventh, and occasionally the pituitary body. The outstanding feature is a *unilateral ophthalmoplegia* which may be partial or complete, external or total. We have not seen the internal form alone. *Exophthalmos* and *ptosis* of the upper lid are part of the paretic picture but should be

* In reviewing the autopsy protocols, it was interesting to note how many of the 297 cases had what was reported as "atheromatous patches," "arteriosclerosis," or "degenerative changes" in the arteries at the base of the brain. There were a number of cases with cerebral hemorrhage, and no demonstrable rupture or point of origin. Considering the method commonly used in removing the brain, it is possible that thin aneurysmal sacs might be destroyed or not noticed.

emphasized on account of their frequency. The various combinations of ocular palsies are given in the case reports and will not be dealt with here. The fifth or trigeminal nerve was involved in 6 cases. The upper branch most frequently suffers, being nearest to the course of the internal carotid, and gives pain and paresthesia or anesthesia over the forehead and around the eye on the involved side. The second or maxillary branch is less frequently pressed upon, giving similar symptoms and findings over the cheek. The third or mandibular branch to the jaw and chin is rarely affected. Involvement of the motor fibers of the trigeminal is also rare, but when present may cause deviation of the jaw, and occasionally the tongue, to the affected side. Actual facial or seventh nerve palsy is also unusual. Decrease or loss of vision may be unilateral or bilateral, due to the close proximity of the internal carotid to the optic chiasm. Direct pressure usually causes unilateral involvement, while hemorrhage may cause decrease in visual acuity on both sides, either by pressure of the clot on the chiasm or by actual infiltration of the blood along the nerve sheaths. Choked discs may be noted on one or both sides, due to the same causes. Loss of vision, of course, may follow an uncorrected ophthalmoplegia, and this may be hard to differentiate from actual nerve involvement. Pressure upon the pituitary body may cause dysfunction of that gland, which, with roentgen evidence of sellar destruction may lead to an erroneous diagnosis of pituitary tumor. Strangely enough, one case (not included in this series, but reported by Cushing in his monograph on the pituitary body and its disorders,—Case xv) had both a pituitary adenoma and an aneurysm of the internal carotid, the latter apparently giving no signs and symptoms and being found only incidentally at post mortem.

These aneurysms apparently do not become large enough to cause general pressure, but the clinical findings incident to increased intracranial tension are well marked following hemorrhages from the aneurysm, their suddeness differentiating them from the ordinary tumor cerebri. The general signs of pressure due to hemorrhage are partly enumerated in Group 1, and there are in addition the better known ones of slow pulse, high blood pressure and rapid respiration, often of the Cheyne-Stokes type. Case A-5 showed these changes well, presumably due to a continuous leak which ended fatally. It should be noted also that fever and leucocytosis usually accompany any intracranial hemorrhage. Any of these neighborhood signs may be placed in Group 1 if they occur suddenly, especially in connection with an epileptiform attack.

3. The signs and symptoms in this group depend upon the various etiological factors, which have been previously discussed. In the first type, hypertension may be found, with the associated symptoms of cardiorenal vascular disease; namely, arteriosclerosis, evidences of renal damage, dyspnea on exertion, edema of the ankles, cardiac enlargement, and tortuosity of the thoracic aorta, often with calcification in the arch demonstrable *in vivo* by the roentgen ray. Ophthalmoscopic examination of the fundi may reveal the tortuous and engorged vessels which are so characteristic. This group includes those aneurysms most apt to be demonstrated by the roentgen ray,—i.e. those of long duration with plaques of calcification in the wall. This group also occurs in the later decades of life when generalized arteriosclerosis is most common.

The endocarditic group is apt to include younger people, the histories showing fewer attacks, usually with a preceding rheumatic fever or acute endocarditis. These aneurysms are apt to be quite small, may be multiple, and in all probability would show nothing on roentgenographic examination, due to their minute size and rapid development.

The aneurysms following trauma are apt to be larger than the preceding group, and if sufficient time has elapsed, may show deposits of calcium in their walls or in the organized thrombi lining the sac. The causative missile or fracture may be demonstrated on the films months or years after the injury. Unless the aneurysmal sac or erosion due to it can be shown, it is natural to suppose that the symptoms are directly due to the injury.

Syphilis probably is not of etiological importance, so that other roentgen evidence of syphilitic involvement, such as an aortic aneurysm, would weigh neither for nor against the diagnosis.

Finally the congenital group is probably a wastebasket where cases with no demonstrable etiological factor may be thrown. We have no evidence for or against such a group except that no cause can be found in certain cases, especially those occurring in young people. There are no peculiarities characteristic of this group.

ROENTGENOGRAPHIC APPEARANCE

The recognition of these aneurysms on roentgen examination is by means of (1) calcification in the wall of the aneurysm, or (2) erosion of the bone adjacent to the aneurysmal sac. In the first, one can see thin plaques of calcium, usually semilunar in shape, with their convexity upward, lying beside the sella, or, should the aneurysm be large, rising above the level of the sella, but just to one side of it. These are fine curvilinear shadows, sharply outlined, occasionally segmented, and easily recognizable as being in the wall of a cystic or rounded structure. They are not to be confused with the flocculent, "spongy" calcification which is seen just above the sella in craniopharyngeal pouch tumors (suprasellar cysts) which have been previously described.[17] The curved shadows are also easily differentiated from the dense hyperostoses seen in meningiomas (dural endotheliomas) which frequently arise in the same location, i.e. from the sheath of the trigeminal nerve or from the sphenoid ridge, and which may give almost identical clinical pictures, except that the suddenness of onset is missing and the remissions or periods of clearing between attacks are absent. (The cerebrospinal fluid will not be found homogeneously bloody or xanthrochromic in these tumors.) The pathology in these, meningeal, tumors as revealed on the films, is one of bone production, often with dense spicules radiating outward and upward, especially if the sphenoid ridge is the point of origin.[19] However, we have seen the appearance of calcification in the wall of one of these aneurysms exactly duplicated by a dermoid cyst of the uncinate region of the temporal lobe. Hence this condition, though rare, should be considered until it is ruled out by the clinical signs and symptoms. No other cysts or cystic tumors have been encountered in this particular location with similar areas of calcification, but there have been several gliomata containing calcification, which has a granular or nodular distribution, quite irregular in outline, and easily distinguishable upon the films.

The erosion due to these pulsating sacs is also fairly characteristic in appearance. It involves or may involve one anterior clinoid, the lateral half of the body of the sphenoid on the same side, and a similar portion of the posterior clinoid. The bone is cleanly destroyed as in aneurysms of the thoracic aorta which erode the vertebra adjacent to it. There is no expansion of the pituitary fossa with displacement upward and outward of the clinoids as in pituitary adenoma, and no apparent depression of the floor of the fossa. The opposite anterior clinoid is not involved and appears smooth in outline and normal in position and there is no pressure atrophy or forward bending of the posterior clinoid as is seen in cerebellar tumors with internal hydrocephalus, or occasionally in large tumors anywhere within the cranial cavity. Finally, there is no increase in the convolutional impressions, even in the cases of long duration.

TECHNIQUE

There are a few points in technique which may be of benefit. The usual procedure which is standard in most laboratories is used,—a spark gap of 4½ to 5 inches, double screens and duplitized "Speed" films, a Bucky-Potter grid, and an exposure of 3 to 4 seconds with 20 milliamperes of current. A fine-focus radiator Coolidge tube is used at a greater target film distance (30 inches) than is customary in most clinics, which gives fine detail. Stereoscopic films, of course, are essential. The first exposure is directed straight through the sella and the second

is from the cephalic shift, so that, when stereoscoped, the line of vision is directed slightly down upon and into the sellar region. If there is questionable erosion of one anterior clinoid as compared with the other, a posteroanterior film may be made with the rays directed along the floor of the anterior fossa. In the majority of cases this will throw the shadows of the anterior clinoids into the shadow of the

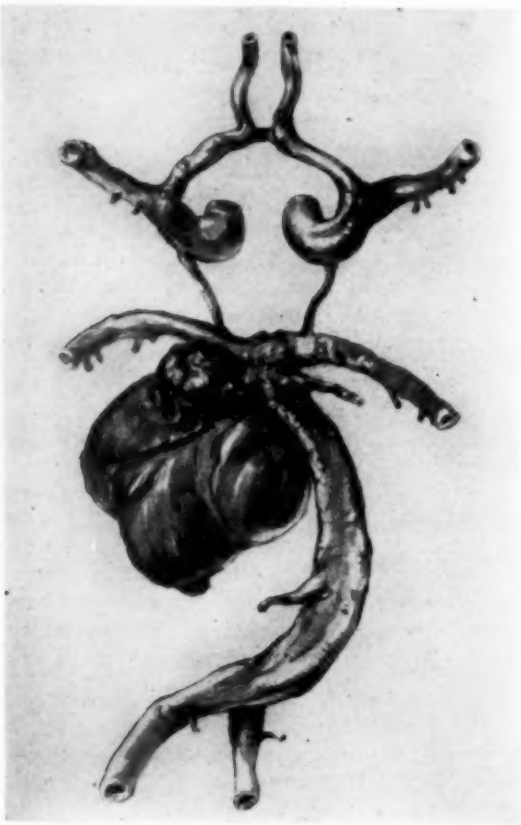

FIG. 2. A sketch of an aneurysm of the posterior cerebral artery after dissection (Case A-1).

frontal sinuses where they can be easily compared. Many roentgenologists will be surprised to see how widely separated the anterior clinoids are, usually 2 or 2.5 cm. If there is questionable thickening of the sphenoid ridge (lesser wing) a posteroanterior exposure in a position half way between a frontal sinus and a Waters or antrum position may be made. This should throw the shadows of the sphenoid ridges directly across the orbits, where they can be more accurately compared.

CASE REPORTS

Our 20 cases have been divided into (A) those confirmed by operation or autopsy and (B) probable cases, as judged by clinical history and findings and roentgenographic appearances, or both. Short abstracts of these cases are presented below. Reference numbers are given when the case has been previously reported.

Proven Cases:

CASE A-1. C. H. B., aged fifty-six, female, surgical number 19715. Seven years ago had a sudden attack of pain in the neck, and vomited. Rapid recovery. Complaint now of being tired, losing weight, and drooping of the left eyelid which occurred suddenly seven months before entry. Subsequent to the ptosis there was staggering, mental confusion, difficulty in swallowing and one spell of coma.

Examination showed paresis of the left third nerve, tenderness in the left temporal region, no exophthalmos, no fifth nor seventh nerve involvement. Mental retardation and incontinence were noted. Left optic disc showed slight choking. Blood pressure 230/140. Wassermann reaction negative. No lumbar puncture. Clinical diagnosis was vascular disease, possibly aneurysm. Death occurred two months later. Autopsy revealed an aneurysm 3.5 cm. in diameter at the origin of the left posterior cerebral artery, arteriosclerotic type. A large hemorrhage compressed the left temporal lobe, pons and cerebral peduncles.

Roentgen findings were slight erosion of the anterior clinoid and a calcified plaque in the region of the basilar artery.

CASE A-2. W. S. C., aged thirty-four, male, medical number 25487, brought to this hospital in coma, with convulsions. One month ago had been found unconscious and taken to another hospital, remained in coma fourteen hours. On recovery could remember nothing of the onset. Had a milder attack one week ago, sudden vomiting and persistent headache.

Examination showed temperature 100°F., respiration 19, pulse 120. Urine showed sugar, no albumen, but red blood cells and leucocytes. Blood count, 5,700,000, W. B. C. 25,000. Both optic discs hazy, no choking, no hemorrhages. Sensory and motor changes could not be determined on account of his condition. Wassermann reaction negative. Blood pressure 170/70. Lumbar puncture showed homogeneously bloody fluid. Clinical diagnosis: ruptured aneurysm. Death occurred nine hours after admission. Autopsy revealed a minute aneurysm (3 mm. in diameter) on the left internal

carotid. No roentgen examination could be made.

Case A-3. F. C., aged thirty-two, female, medical number 5430. Admitted in coma, following a sudden vomiting attack and a "fainting spell." (Had taken cocaine as was her habit, according to relatives.) No history of any previous attacks. Examination showed external strabismus, left eye, no ptosis, no exophthalmos. Pupils equal. Temperature 101.2°F., pulse 64. Urine clear. Fresh hemorrhages in both fundi, involving the disc on the left, nasal side on the right. (These increased in size under observation of three hours.) No choking. Blood pressure 188/118, increasing to over 300 (systolic) one hour later. Lumbar puncture (done on account of a stiff neck) showed very bloody fluid. Wassermann, blood and spinal fluid, both negative. Blood urea nitrogen normal. Death three hours after admission (ten hours after onset).

Autopsy showed a small aneurysm "the size of a pea" on the left internal carotid, with a large hemorrhage, some of the blood infiltrating the optic nerves. (See reference 8; and 13, Case 5.) No films obtained.

Case A-4. B. H., aged fifty-two, female, surgical number 13075, came in with a severe headache of one week's duration, sudden in onset, with vomiting, drowsiness and double vision. Has had "high blood pressure" for seven years, headaches for one year, with "pressure" in the back of the head, retraction of neck, and pain radiating down the back. Also vomiting without nausea, staggering, failing vision and poor memory.

Examination. Complete ophthalmoplegia on right (except external rectus) with ptosis and fixed pupil. Exophthalmos, bilateral, more on right. Pain over right temple and around eye and face, no anesthesia nor facial paresis. Temperature, pulse and respiration normal. Wassermann test not done. No lumbar puncture. Fundi of eyes showed slight swelling of both optic discs on admission, and two days later (after a convulsion and gradually developing coma) definite choked discs with hemorrhages on the left. The diagnosis was not made clinically. A right-sided decompression revealed a subdural hemorrhage. Autopsy disclosed an aneurysm of the right internal carotid, 3 mm. in diameter, and many atheromatous beads on the other vessels. No erosion of bone. Blood within the sheath of the left optic nerve. Right oculomotor nerve compressed.

Our plates showed a normal sella, no erosion and no calcification. (See references 12, Case 1; and 13, Case IV.)

Case A-5. C. A. H., aged forty-five, female medical number 23490. Admitted in coma, twenty-four hours' duration, sudden onset with convulsions and vomiting. A previous convulsion was noted six months before, with loss of sight in left eye and impaired vision on right, both due to subretinal hemorrhages. For two years has had nocturia, dyspnea, headaches and hypertension.

Examination showed pupils equal. Reaction normal, both eyes rotated upward. Fundi of eyes showed arteriosclerotic vessels, with acute hemorrhages, but no choking. Blood pressure 140/90. Wassermann reaction negative. Lumbar puncture gave homogeneously bloody fluid, and resulted in marked mental clearing and complete relief of coma. Three hours later, however, there was another convulsion with coma, blood pressure rose to 180/100, respirations rose, pulse fell, temperature rose rapidly and the patient died, in spite of a second lumbar puncture. The autopsy showed an aneurysm of the right internal carotid, 1.6 × 1.3 cm. in diameter, arteriosclerotic type, which had ruptured. There was marked pressure on the optic chiasm, with displacement of the right optic nerve. Diagnosis not made clinically.

No films were secured in this case, due to the condition of the patient (see reference 16).

Case A-6. Mrs. M. R., aged fifty-two, no number, was referred to this clinic with a tentative diagnosis of pituitary adenoma. She had had several attacks of blurred vision in the right eye a year before, with a sudden loss of vision, and pain down the right side of neck at the same time. The urine showed a trace of albumen, and a few casts. Wassermann reaction negative. No diagnosis was made, except that it was not a pituitary adenoma, and she was sent home. A month later there was a sudden severe headache, transient diplopia and a questionable weakness of the left arm and leg. A right frontal bone-flap was turned down by a neurological surgeon, disclosing "a pink tumor arising from the sphenoid ridge, soft in consistency, and undoubtedly a glioma." No attempt was made to remove it. Two weeks later she died suddenly, and the autopsy revealed an aneurysm of the right internal carotid, 2 cm. in diameter, which had ruptured. It compressed the pituitary body and the chiasm, almost cutting off the right optic nerve, and had partly eroded the sella.

Roentgen examination, as reported by Dr. Eugene Caldwell, showed erosion of the right half of the posterior clinoids. No films were made here.

Case A-7. A. S., aged twenty-six, female, surgical number 6433, was admitted because of a severe right-sided headache, sudden onset seven weeks previously, with a concomitant

ptosis of the right eye-lid, diplopia, vomiting and vertigo.

Examination showed a complete ophthalmoplegia on the right, loss of the corneal reflex, a large fixed pupil, and enophthalmos. There was sensory loss over the right fifth nerve area and deviation of the jaw to the right. Blood pressure on two occasions was 170/110 and 200/112. Lumbar puncture negative. Wassermann (blood and spinal fluid) both negative. Fundi of eyes normal. Clinical diagnosis meningioma trigeminal nerve sheath. Operation disclosed an aneurysm "the size of a walnut." Death occurred nine months later after a progressive down-hill course. A single glass plate showed a normal sella, but there were faint areas of calcification beside it (see reference 9; and 13, Case 3).

Case A-8. J. S., aged thirty-five, male, medical number 12604, had a twelve days' history of severe occipital headaches, beginning suddenly, with vomiting, fever, one convulsion and several delirious spells. Examination showed pupils normal, no paralyses or paresthesias. Fundi of eyes showed slight blurring of the right optic disc. Because of a stiff neck, positive Kernig and Babinski signs, and increased reflexes, with the fever, lumbar puncture was done, releasing bloody fluid under increased pressure. No growth was obtained, but as there was a mild epidemic of cerebrospinal meningitis, a course of antimeningococcus serum was started. Wassermann reaction negative. Subsequent lumbar punctures, four in number, yielded bloody fluid. Death occurred during a convulsion. The autopsy revealed a small aneurysm at the origin of the right anterior cerebral artery, 6 × 7 mm. in size, with blood clots and a diffuse hemorrhage around it and into the ventricles and the brain itself. The vessels were not diseased.

As the patient had been isolated, no roentgen examination was made (see reference 13, Case 6).

Case A-9. F. S. W., aged fifty-eight, female, surgical number 22647, complained of two severe attacks of pain involving the right forehead, eye and face, sudden in character, one year and eight weeks ago respectively. The history, however, showed several transient attacks of diplopia, the first one ten years ago. Examination showed exophthalmos, paresis of the external rectus, anesthesia of the cornea, a small sluggish pupil and paresis of the masticatory muscles, all on the right. Fundi of eyes were normal. Blood pressure 150/90. Wassermann reaction negative. No lumbar puncture. Clinical diagnosis was meningioma of the right trigeminal sheath. Operation, however, revealed an aneurysm of the right internal carotid. After placing a ligature, the sac was opened and the laminated clot removed, in an attempt to do an aneurysmorrhaphy. A gush of blood necessitated tying the ligature, the cavity was filled with muscle and the sac sewed up. A left hemiplegia ensued, which gradually cleared up with a partial return of sensation, and the patient was discharged two months after operation, walking with the aid of a cane. She died at home six months later, autopsy revealing an aneurysm 3.5 cm. in diameter. There was marked erosion of the sella and considerable necrosis of the right hemisphere.

Roentgen examination before operation showed definite erosion of the right side of the sella, including anterior and posterior clinoid, but no calcification. Postoperative films revealed nothing further.

Case A-10. Mrs. W. W., aged sixty-nine, not admitted to the clinic, but seen in consultation outside by Dr. Horrax. Her history showed a questionable attack of rheumatic fever, and a definite respiratory infection, the latter just preceding her present illness. This began with a marked pain in the right eye and between the eyes. A month later she suddenly fell to the floor unconscious. A second attack was ushered in by a sudden pain in the right eye, occiput and neck, nausea and vomiting and an irregular pulse. She remained stuporous longer than usual (several months). Examination showed ptosis of the right eyelid, paresis of the oculomotor nerve and a fixed pupil on the right. Ophthalmoscopic examination was difficult because of cataracts, but no hemorrhages or choked disc were seen. Definite impairment of sensation was noted over the right trigeminal distribution. Urine clear. No Wassermann test done. Pulse 50 to 120. Blood pressure not noted. Lumbar puncture urged but refused by the patient. Clinical diagnosis, aneurysm of the internal carotid (Dr. Horrax). During a third attack, two years after the first one, the patient died. Autopsy disclosed an aneurysm 2 cm. in diameter, apparently arising from the posterior cerebral artery. It had ruptured, and there was an extensive hemorrhage over the surface of the brain.

Roentgenograms of the brain post mortem showed no demonstrable calcification.

Case B-1. Mrs. D., aged sixty-eight. Not admitted to the clinic but seen in consultation with Dr. Mixter. Her history appears quite typical, with pain on the right side of the face, buzzing in the right ear and diplopia six years ago. Since then there have been unilateral headaches, failing vision on the right, pain in the right cheek, bleeding from the right nostril, and lately a "peeping" sound in the right ear

synchronous with the pulse beat. Examination showed complete third nerve palsy on the right, ptosis of the lid, right fifth nerve involvement (sensory and motor), but no changes in the retinae. Blood pressure 150/90 and later 120/90. Wassermann reaction negative. Urine clear. Blood normal. Lumbar puncture not done. Clinical diagnosis aneurysm right internal carotid.

Roentgenographic examination (by Dr. R. C. Stewart of Lowell, Mass.) showed a very distinct curvilinear shadow rising from the right middle cranial fossa well above the sella, forming almost a complete circle and apparently being calcification in a cyst wall or in a cystic structure. Diagnosis, aneurysm of the right internal carotid artery.

Case B-2. G. W. B., aged fifty-four, male, surgical number 3665, had a sudden severe right frontal headache six weeks before entry, with a sudden ptosis of the right eyelid a week later. Two days before entry there was loss of vision in the right eye followed by unconsciousness, also sudden in onset. There was a history of rheumatic fever ten years ago.

Examination showed complete third nerve paralysis on the right, with a dilated fixed pupil. The left sixth nerve was weak. No exophthalmos. Urine was clear at first, later showing a trace of albumen, and a few casts. Blood urea nitrogen 22 mgm. per 100 c.c. Blood pressure 205/115. Fundi of eyes showed subhyaloid hemorrhages, no choking, right disc blurred. Lumbar puncture gave homogeneously bloody fluid, five days later brownish fluid "containing old blood." Wassermann (blood and spinal fluid) negative, and again negative after a provocative test.

The patient was discharged improved and died outside two years later. No autopsy was performed.

Roentgen examination showed a normal sella, no erosion of the clinoids and no plaques of calcification.

Case B-3. W. R. B., aged fifty-one, male, medical number 19721, was admitted in a dazed semicomatose state, following a sudden acute headache twelve days before, with projectile vomiting, coma, anuria for twenty-four hours, and convulsions. There had been infrequent temporary headaches, occipital, with buzzing in the ears, for the past year.

Examination showed ptosis and exophthalmos on the left, with a third nerve palsy. Left pupil dilated and fixed. No fifth nerve involvement. Fundi of eyes showed slight choking of the left disc. Pulse 60, temperature 99° to 101°F., respiration Cheyne-Stokes in type. Condition improved after lumbar puncture (which yielded bloody fluid) and the pulse rose to 100, with disappearance of the headache. Ocular movements returned but the ptosis remained. Wassermann (blood) negative, spinal fluid, double plus. Patient was discharged to the out-door department and was well a year later.

Skull films (No. 26499), showed increased vascular channels in the cranial vault, no erosion of the sella, and plaques of calcification in the region of the basilar artery.

Case B-4. F. K., aged seventy-seven, female, surgical number 18735, was admitted with a history of longer duration than the others. Twenty years ago there was a partial ptosis of the right lid, with periodic attacks of pain in the right fifth nerve area ever since. The right external rectus was suddenly paralyzed thirteen years ago. Five years ago there was a sudden headache with pain in the right eye. At examination there was right ocular palsy with extreme internal strabismus, no ptosis. Pupil fixed. Sensory loss over all three divisions of the right fifth nerve, and a right-sided hemiatrophy of the face. Blood pressure 230/120. No lumbar puncture. Fundi of eyes showed marked arteriosclerosis. Discharged, no operation. A year later she reported several severe attacks of pain, sudden onset, gradually disappearing. Ocular and trigeminal involvement stationary.

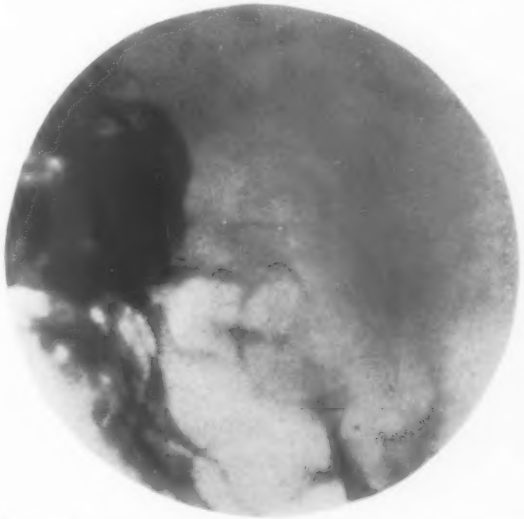

Fig. 3. Roentgenogram of the sella in a case of aneurysm of the internal carotid, showing the characteristic semilunar areas of calcification (Case B-4).

Roentgen films (No. 28618) showed characteristic findings,—erosion of the lateral half of the sella, with large semilunar areas of calcification beside it, rising above the level of the clinoids.

Case B-5. A. A. W., aged forty-four, female, surgical number 21178, was admitted because of a sudden attack of unconsciousness with vomiting. There was a persistent headache following this, with pain radiating to the neck.

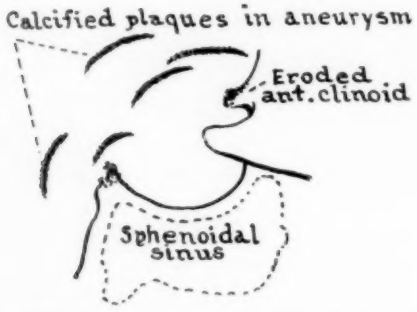

Fig. 4. Diagram of Figure 3 to show the location and character of the calcified plaques in the wall of the aneurysm.

Examination showed ptosis of the right lid, no exophthalmos or ocular palsies. Fundi of eyes showed bilateral choked discs with hemorrhages. Blood pressure 172/90, later 148/92. While under observation there was an epileptiform attack, blood pressure rising to 204/96, temperature to 102.2°F., and lumbar puncture yielded a homogeneously bloody fluid. Twelve and twenty-four days after the attack the spinal fluid was still xanthrochromic. The patient gradually improved and was discharged without operation.

Skull films (No. 32651) showed no characteristic changes.

Case B-6. J. Z., aged fifty, male, surgical number 13554, complained first of stiffness in the neck. Two days later there was a sudden right frontal pain, then ptosis of the right eyelid, strabismus and diplopia.

Examination showed a total oculomotor palsy on the right, no sensory disturbances. Spinal fluid was homogeneously bloody, and twenty-one days later xanthrochromic. Fundi of eyes showed nothing abnormal. Wassermann reaction negative. Ptosis and headache improved under rest but later recurred. Discharged unimproved, no operation. Two years later condition was stationary.

Skull plates (No. 19847), showed no erosion of the sella or abnormal calcium deposits.

Case B-7. J. L., aged sixty-four, female surgical number 23451, was seen first in the out-door department. She was sent in because of severe headaches, insomnia, nervousness, mental deterioration and several epileptiform attacks. The history is unreliable on account of the patient's mental difficulties, but a relative and her physician told of attacks of unconsciousness associated with convulsions, lasting fifteen minutes to two hours. There is apparently an aura but no memory of the aura or attack afterward.

Examination showed an internal strabismus, both pupils large and irregular and reacting poorly. Ocular movements suggest weakness of the external recti. No ptosis or exophthalmos. No fifth nerve involvement. Blood pressure 107/90. Ophthalmoscopic examination impossible on account of early cataracts. Heart enlarged, aorta quite tortuous. Wassermann reaction negative. Urine normal. Lumbar puncture gave clear fluid under no tension (last attack three months ago). Clinical diagnosis—cerebral arteriosclerosis.

Roentgen examination (No. 36452) showed erosion of the lateral half of the posterior clinoid, with two curved shadows of calcification, one beside the sella and the other over it. Findings suggested an aneurysm of the internal carotid.

Case B-8. M. G., aged sixty-two, female, medical number 25551, is now on the medical service under observation. She was in the hospital five years ago with a pain in the left face and neck, bilateral deafness, and a left facial paralysis. Since then there was a sudden

Fig. 5. Case B-1. Large seminular areas of calcification rising above and to the side of the pituitary fossa. Note erosion of anterior clinoid. (Roentgenogram by Dr. R. C. Stewart of Lowell, Mass.)

diplopia lasting three months. She now has a left facial paralysis, bilateral deafness (duration thirty years), generalized arteriosclerosis, and a pulsating mass at the angle of the left jaw. Blood pressure 225/100. Wassermann reaction negative. Fundi of eyes show arteriosclerotic vessels and some exudate. Temperature normal. Pulse varies from 60 to 100.

Clinical diagnosis arteriosclerosis, aneurysm of carotid in neck, and questionable aneurysm, intracranial portion.

Skull films (No. 19885), show no erosion of the sella. There is calcification in both internal carotids which can be traced throughout their entire intracranial course. At their first forward bend there are bilateral bulges so that the artery rises above the level of the center of the pituitary fossa. Findings are compatible with small bilateral aneurysms of the internal carotids.

CASE B-9. A. B., aged thirty, female, medical number 25589, is also on the ward under observation at present. Six weeks ago there was a sudden attack of nausea, vomiting, and headache, followed by general malaise, with a similar attack three weeks later, the headache predominating, and two days after that a convulsion.

Examination showed a stiff neck, a slow lateral nystagmus, slight fever, rapid pulse, a leucocytosis of 26,000, and a blood pressure of 165/110. Fundi of eyes showed hyperemia and engorged veins suggesting obstruction on the nasal side. Wassermann (blood and spinal fluid) both negative. The spinal fluid showed bright red blood two days after the first attack, again three days after the convulsion, and was respectively "wine-colored" and then xanthrochromic thirteen days and twenty-eight days later. The clinical impressions were pachymeningitis hemorrhagica, ruptured aneurysm, or ordinary hemorrhage.

Our films showed erosion of the right half of the posterior clinoids and calcified areas in the course of the internal carotid.

CASE B-10. C. L., aged seventy-two, female, medical number 25608, also on the ward at the present writing, has a long history of hypertension, known for ten years, and evidences of chronic nephritis. She was on the surgical service eight years ago for osteomyelitis of the hip. Her history is not characteristic, being essentially that of hypertension.

Examination showed retinitis, enlarged heart, blood pressure varied from 230/90 to 275/130. Temperature and pulse normal. Fundi of eyes showed retinal arteriosclerosis and retinitis, with hemorrhages. Wassermann reaction negative. No lumbar puncture.

Roentgen examination (No. 6326) showed erosion of the right anterior clinoid, with calcification in both internal carotids, and the basilar arteries. The carotid in the neck also showed marked calcification. Findings indicated a cerebral arteriosclerosis, and possibly an aneurysm causing erosion of the clinoid.

DISCUSSOIN

These cases show several interesting points which should be stressed: (1) The striking similarity in the histories and physical findings, the details of which have already been enumerated; (2) the predominance of the arteriosclerotic or degenerative group, the occasional occurrence of unexplained aneurysms ("congenital"), and those of embolic or mycotic origin, and the extreme rarity of anything suggesting syphilitic involvement, and (3) the value of the roentgen examination in the diagnosis of this condition. Statistics of positive roentgen diagnosis are unfair, because several of the proved cases were seen in the days of glass plates and uncertain gas tubes. However, we have roentgenographed all of the autopsy specimens we could find and several of the most promising ones showed no calcification. It might be justly said that in 25 per cent of the cases in which skull films were secured the diagnosis was possible from the roentgen examination and that in another 25 per cent our findings would support the clinical impression. In Group A, no examination was made in 5 of the 10 proved cases. In the remaining 5 one was frankly negative, one was definitely diagnostic and 3 showed changes which might be important or not, depending upon the history. In Group B, of 10 probable cases, all of whom were roentgenographed, 6 present appearances on the films which lead to a presumptive diagnosis of aneurysm, 3 are frankly negative and one is questionable. The predominance of positive findings in the latter group is probably due to two factors: (1) Having recognized this condition as a clinical entity with definite roentgen evidence in certain of the cases, we are on the watch for it, and (2) the present day films give us so much detail that we are enabled to see the changes when they do occur.

CONCLUSIONS

1. Aneurysm of the arteries at the base of the brain is not a rare condition.

2. It is possible to make an ante mortem diagnosis of aneurysm of these cerebral

arteries from the history, clinical findings and roentgenographic evidence. The two methods should be carefully coordinated and the value of each estimated before arriving at any conclusion.

3. Prognosis may be estimated more accurately in those cases which have positive roentgen findings, qualified by the type of lesion and the duration of symptoms.

4. No definite form of therapy has been established, although in one patient, in whom the lesion was unexpectedly exposed at operation, an aneurysmorrhaphy was attempted.

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CONGENITAL DIAPHRAGMATIC HERNIA

WITH A REPORT OF SEVEN CASES WITH AUTOPSIES

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As early as 1698, Riverius reported a case of congenital hernia of the diaphragm. In 1899 Grosser compiled a series of 433 cases in which a congenital origin could be demonstrated in 232. Due to the roentgen ray, this condition is at present easily diagnosed, but prior to 1908 Arnsparger states that the condition had not been recognized during life in more than 10 instances.

Diaphragmatic hernias, like those involving any other portion of the abdominal parietes, are simply protrusions of one or more of the abdominal viscera into the thoracic cavity, through a congenital or acquired opening. These hernias may be true or false, depending upon the presence or absence of a sac.

VARIETIES OF CONGENITAL DIAPHRAGMATIC HERNIAS

I. *False Congenital Diaphragmatic Hernia.* This variety is by far the most common and according to Lupman constitutes 87 per cent of the congenital hernias. The hernial contents pass directly through a congenital opening or through a dilated normal opening.

II. *True Congenital Diaphragmatic Hernia.* These differ from the previous group in that this variety has a definite sac usually made up of a thin layer of pleura and a layer of peritoneum, which layers precede the hernial contents into the thorax.

III. *Diaphragmatic Eventration.* This term was applied by Petit in 1790 to the condition of chronic, idiopathic, unilateral, elevation of the diaphragm described by him.

ETIOLOGY

The false congenital diaphragmatic hernia results from an impediment of the normal closure of the diaphragm during intrauterine life. An opening of variable size admitting communication between thoracic and abdominal cavities is the result. Klebs reports a case where the diaphragm was totally absent and yet the child lived for six years. However this is not the rule, for the opening is usually much less extensive.

There are certain regions of the diaphragm that are commonly the site of congenital hernias due to an arrest or defect in development:

(1) Larrey's space or foramen Morgagni, which is a triangular area between the pars sternalis and pars costalis of the diaphragm;

(2) Foramen Bochdaleki. This is the common site and it is a space on either side between the pars vertebralis and pars costalis. Grossnitz has shown from a study of comparative anatomy that this area is the last portion of the diaphragm to be closed and he found that small defects invariably occur in this situation. The larger the opening, the greater is the involvement of the lateral and finally of the ventral areas of the costal portions of the diaphragm. In extreme cases almost the entire half of the diaphragm may be missing, only a vestige of muscle extending from the sternum laterally and to the chest wall, remaining. This simulates the case reported by Klebs. The various grades of congenital defect therefore may be regarded as different degrees of arrested development.

Of the various theories advanced to explain the influences operative in fetal life, in restricting the normal closure of the diaphragm, that given by Laterjet and Jaricot is perhaps the most plausible one. They state that since that portion of the diaphragm that is the last to close, is the most poorly vascularized, only a slight degree of abnormal pressure here would suffice to cause nutritional disturbances with a resulting arrest of development. The left half of the diaphragm is the side most commonly involved. Eppinger gives the following statistics:

	Right	Left
Hernia spura	34	527
Hernia vera	21	53
Eventratio	2	15

Other authorities give a ratio of 8 to 1 for left-sided hernias as compared to those involving the right side. The preponderance of left-sided hernias may be accounted for by the presence of the liver on the right side lying in close proximity to the diaphragm shielding any defect that may exist and in addition playing the part of a bulwark to defend the right side of the muscle during development from any undue pressure from below. There are in addition two fibrous bands at the right side of the diaphragm which do not exist at the left, thus further strengthening the right half of the muscle. The left half of the diaphragm is distinctly weakened from the beginning by two distinct pouches, namely, a pouch for the spleen and the other, the cul-de-sac for the stomach to rest in. In addition, most of the natural foramina are in the left half of the diaphragm, which factor also plays its part in further weakening that part of the muscle.

Where the size of the natural foramina are excessively large, hernias may also develop and add to the number of sites for congenital diaphragmatic hernias.

(3) The opening through which the sympathetic nerve passes may be the site of a hernia. Bowditch reports but two such cases in his "Treatise on Diaphragm Hernias."

(4) At the hiatus esophagus, where the surrounding musculature of the diaphragm is loosely attached to the esophagus and where in addition, the foramen may be exceedingly large; only 3 such cases have been reported by Bowditch.

Hans Eppinger summarizes the etiological factors for congenital hernias as follows:

(1) Embryological defects of the diaphragm as arrested development of a portion.

(2) Excessive size of the natural foramina.

(3) Weakness of muscular layers, etc.

In the second variety of congenital diaphragmatic hernias, namely, the true congenital hernias, the same etiological factors have been at play but there was a congenital arrest of development occurring at a later period than in the preceding group. The weakest portion of the membranes, namely, the most recently closed is the site for the thoracic protrusion and since it is as yet, too early for a growth of muscle sufficiently strong to resist the pressure, a true hernia with its sac of peritoneum and pleura is the result.

As regards the aperture of diaphragmatic hernia, the rounded, oval or semicircular tendency is very manifest and has been repeatedly observed. The anatomical structure of the diaphragm will explain this very satisfactorily. Because of the circular direction of the muscular fibers, their contraction would tend to produce a rounded aperture modified perhaps by other circumstances such as the degree of deficiency into an oval or semicircular opening.

CONTENTS OF THE HERNIA

Lacher states that every abdominal organ excepting the genitals, bladder, and rectum, have been found at least once within the thoracic cavity. Bowditch gives the following statistics:

Organs Found in Chest	Thorax		
	Left	Right	Doubtful
Stomach	34	4	6
Large intestines	26	5	8
Small intestines, part	21	4	4
Liver, whole or part	8	7	
Gall-bladder		1	
Pancreas	4		2
Spleen	11		2
Omentum	24	3	3
Mesentery	1		1
Kidney		2	

SYMPTOMS

The symptoms of a congenital diaphragmatic hernia are very variable, for, in some cases, symptoms may come on soon after birth, while in others, there may be no complaints whatsoever and the patient may reach adult age before the condition is discovered, in many instances accidentally.

In Cases I and V reported below, the symptoms came on very soon after birth. In Cases II and III the children were approximately one year of age before any symptoms came on. Case IV is an adult whose occupation was that of a blacksmith and even under such conditions he had not complained until he reached the third decade of life. Case VII is a woman who up to the present time has no complaints whatsoever.

In giving a general discussion of the symptoms that may occur with a congenital diaphragmatic hernia it is probably best to divide the subject up into symptoms before, and during the fatal attack.

Previous to Fatal Attack. The symptoms may be entirely absent, they may be very mild and simulate some gastric disturbance or they may be grave and terminal.

Dyspnea is a rather common complaint in these cases and the degree is dependent upon the amount of pulmonary compression. From the cases of Bowditch there is enough evidence to prove that the greatest degree of hernia may exist on one side and the patient may be muscular and able to do the hardest work, though liable at times to attacks of dyspnea accompanied by cyanosis. In two of those cases Bowditch states that the patients were very muscular. In Case IV reported below, the patient was also very well developed and muscular. This fact is quite in accordance with what is seen in other conditions where the disease consists of a merely local disturbance without the constitution being necessarily affected. One can therefore conclude that although these patients are suffering from diaphragmatic hernia and may have at times troublesome and dangerous symptoms, nevertheless when they arrive at adult age, there is nothing to prevent a full development of the muscular and adipose tissue. However this does not follow in children, for they are usually very thin and underdeveloped.

The gastric symptoms that some of these patients complain of may be just "weakness," liability to oppression, fullness after eating, or nausea and vomiting. The tendency to vomit usually commences soon after birth and continues with more or less frequency until the fatal attack. In all the cases where gastric symptoms were noted, autopsy or roentgen examination revealed the stomach either wholly or partly in the chest. Abdominal pains or colics were often associated with the above gastric symptoms and they were usually very violent. The colic would occur irregularly or very frequently following the ingestion of excessive amounts of food. The pain was usually located in the upper abdomen near the diaphragm or else it would be referred to the site of the stomach.

Symptoms During the Fatal Attack. If the symptoms occur very soon after birth, it will be noticed that the breathing is very shallow and the infant is cyanotic. Artificial respiration may be tried in the hopes of producing resuscitation, but there is not much improvement and at times it may even aggravate the existing manifestation. The cry is very weak and the child may even develop convulsions thereby simulating some cerebral condition such as trauma and hemorrhage occurring during the labor.

In older individuals during the fatal attack they may show short and quick respirations, panting, interrupted breathing or frequent and very labored breathing. Hiccough which is supposed to be a symptom indicative of disease of the diaphragm occurred in only one-third of the cases reported.

The voice may show changes due most likely to pressure very high up on the trachea. In one of the reported cases where the voice had a pecular tone to it, the colon filled with meconium was pushed between the aorta and the spine and pressed upon the trachea as high up as the first rib.

Vomiting may also occur and help close the scene. The vomiting may be gastric and even fecal. In these patients there is most often a strangulation of the stomach alone or stomach and intestines.

It is during this fatal attack that we most often find the patient presenting all or some of the signs of shock, although in some instances a patient will go into shock during some of the more severe previous attacks.

Physical Signs. If the patient is a newborn baby there may be great difficulty in

eliciting any positive physical signs except that the heart may be pushed over somewhat to the right. In older patients, in addition to a displacement of the heart, there may be a hyperresonant note over the chest occupied by the hernial contents, the breath sounds may be distant and one may hear various gurgling and tinkling sounds. Litten's sign may also be absent.

REPORT OF CASES

Case I. Male baby delivered after an uneventful labor, by Dr. Speiser. The total duration of the labor was only ten hours. Immediately after the delivery of the child, there was a delay in the onset of respiration. Mucus in the mouth and pharynx was removed and then artificial respiration was begun, when we found that slapping its soles and buttocks did not produce the desired effect. The child began to breathe and finally cried, but it was a weak cry. The cyanosis which was present immediately after birth, cleared to a moderate degree. The child did not get any worse nor did it improve any until seven hours after delivery when the breathing became more shallow and the cyanosis increased considerably. Artificial respiration was again instituted with a lung-motor and the breathing became just a little improved as did also the cyanosis, but the cry was still very weak. This improvement lasted only half an hour when all symptoms became aggravated and the child expired.

Roentgen Findings. Upon roentgen examination we were able to see the contents of the abdominal cavity protruding into the chest. The lungs were apparently entirely on the right side, compressed into a small area occupying the right apex of the chest cavity. Trachea and bronchus were apparently normal, the right bronchus having three bifurcations and the left two. The heart was apparently normal in size and shape and displaced into the right chest cavity. The esophagus was normal in position, shape and size.

The left chest cavity was occupied by the stomach, small gut and practically the entire colon. The left diaphragm showed a deficiency through which the viscera protruded. The right half of the diaphragm was apparently normal.

The abdomen contained the liver, lower portion of colon, sigmoid and rectum. The bismuth injection of the abdominal viscera confirmed the above findings with apparently a malformation or defect in the diaphragm and position of the greater part of the gastrointestinal tract.

Autopsy. (Dr. Cotter.) Infant—weight about 8½ pounds, well nourished, no bruises or scars, hypostasis present, *rigor mortis* set in.

On opening the chest, most of the abdominal organs were found filling the entire left chest and part of the right side of the chest.

Right side: Lungs, three small lobes were found filling a small part of the posterior chest.

Left side: Left lung, two minute embryonic buds could be seen coming from the tracheal hilus.

Heart: Normal in size, pushed to the right side of the chest and apex pointing to the left. Fetal circulation is still present.

Stomach is in left chest just above the left diaphragmatic wall, normal in size. Entire small intestine surrounds the stomach, and fills the left and part of the right chest. Spleen was found lying between the intestines in the left chest. It consisted of two parts—an accessory lobe. The ileocecal junction was at the diaphragmatic opening where an elongated appendix extruded. In the left leaf of the diaphragm was a more or less circular opening which was bounded posteriorly by the 8th, 9th, 10th and 11th ribs and anteriorly by a thin rim 1.5 cm. of diaphragm. Through this opening the abdominal contents protruded. The right leaf of the diaphragm was normal in size and shape.

Liver was enlarged and ptosed. The gall-bladder reached the level of the umbilicus.

Kidneys: Right, fetal lobulations present, normal in size and freely movable about the abdomen; left, normal and fixed.

Ureters: Right, kinked; left, normal. Both led to the trigone of the bladder.

Bladder: Normal.

Thymus: Normal in size and position.

Brain: Normal.

Cause of Death: Asphyxiation and cardiac failure, due to pressure of herniated abdominal contents on the heart and lungs.

Case II. (From City Hospital, Welfare Island.)

July, 1921. H. G., aged one year and three months. This child had been admitted to the hospital with a diagnosis of congenital syphilis. The child appeared very pale but no dyspnea nor cyanosis was present. It was fairly well nourished and well developed.

Physical examination was negative until the chest was reached where impaired resonance and a diminution to absence of breath sounds were elicited over the left lower chest both anteriorly and posteriorly. In the abdomen both liver and spleen were very much enlarged.

The child expired one day after admission. The Wassermann test was negative.

Autopsy. (Dr. Benj. Schwartz, deputy chief medical examiner.)

Body is that of a white, male child appearing to be about the age given. Height 2 ft., 6½ in. weight by scale 16½ lb. Hair, brown. *Rigor mortis* present in jaw and lower extremities, absent in upper extremities. Hypostasis developed. Pupils equal normal in width.

Teeth: Upper jaw, four incisors present, first bicuspid right and left of upper jaw are erecting, lower jaw, two median incisors, all other teeth absent.

Chest: Somewhat greenish

Abdomen: Peritoneal cavity free from fluid.

Liver extends down into pelvis.

Spleen is large also extending into false pelvis. In the abdominal cavity the stomach is present between the liver and spleen. The only part of the intestines present in the abdominal cavity are descending colon, sigmoid and rectum. There is an opening in the left side of the diaphragm about one inch in extent, through which the descending colon passes.

Diaphragm: Right side upper margin at 6th rib, left side upper margin at the 7th rib.

Chest: Left pleural sac contains the left lung which is markedly collapsed; also small and large intestines. Right pleural sac was free from fluid and adhesions, the lower lobe of the right lung has three superficial fissures. Lung on section, congested. Left lung has three lobes, the lower lobe and the upper half of the middle lobe being markedly atelectatic.

Heart: Pericardial sac normal; heart's blood fluid; valves normal; foramen ovale closed; aorta normal

Liver capsule smooth, on section firm, normal in appearance, weight 360 gm.

Spleen on section studded with numerous prominent follicles, weight 63 gm.

Thymus: Weight 28 gm. consisting of glandular tissue; *pancreas* normal; *adrenals* normal.

Kidneys: Normal in size, marked fetal lobulations. On section normal. Pelvis and ureters normal.

Bladder, normal.

Stomach and esophagus, normal.

Intestines: Peyer's patches and solitary follicles are prominent in the ileum. Appendix, normal. Large intestines normal.

Neck: There are no marks on the neck. There is no hemorrhage in the skin or muscles beneath the skin of the neck.Tongue, normal. Tonsils somewhat enlarged. Larynx and trachea normal.

Head: Scalp normal. Skull and brain normal.

Cause of Death: Congenital diaphragmatic hernia. Small and large intestines in left pleural sac.

Case III. (From Bellevue Hospital.)

August 11, 1920. A. L., aged one year.

Chief Complaint: Dyspnea and cyanosis. inability to take food, from natural causes. No injury other than a chest aspiration before roentgen examination revealed a left sided diaphragmatic hernia with the left chest entirely filled with intestines. Chest aspiration done July 25. Up until two weeks before admission the mother had not noticed anything peculiar about the child. At that time the child began to lose weight rapidly, vomited considerably and had some diarrhea. When the child came to the hospital it was very cyanotic and dyspneic.

Autopsy (Dr. Schwartz.)

The body is that of a male, white child, one year old, 2 ft., 4 in. in height and weighing 14 lb. There is a marked post mortem stasis. *Rigor mortis* is present. There is an area of greenish discoloration over the anterior aspect of the chest. On opening the peritoneal cavity it is found to contain a hugely dilated stomach, which fills up the greater portion of the abdominal cavity. The diaphragm is at the level of the 4th rib on the right and the 6th rib on the left. The posterior portion of the left side of the diaphragm is absent, leaving a hole which admits four fingers easily.

The left kidney partly fills this opening, the upper half being in the thoracic cavity and the lower half in the abdominal cavity. It is through the remainder of this space that the intestines pass up into the thorax.

Chest: On opening the chest cavity the left side of the chest is found to contain practically all of the small intestines and considerable of the large intestine.

Lungs: The right lung is about normal in size. The left lung is displaced to the right and upward. It is very small and compressed and contains three lobes. The lower lobe is completely collapsed and contains practically no air.

Heart is markedly displaced to the right, the apex being about in the left parasternal line, the right border at about the right nipple line, the heart is otherwise normal.

Liver is normal in size and position. Section reveals normal liver tissue.

Spleen is enlarged, the lower pole being about 1½ in. below the costal margin. The whole spleen is displaced forward and downward.

Kidneys: The right is normal in position, the upper pole of the left is in the thoracic cavity.

Adrenals normal.

Pancreas is normal in position and on section.

Stomach is very much dilated and fills most of the abdominal cavity. It is rotated to the right so that the duodenum seems to come off posteriorly, turns sharply upward and to the

left. The ileum runs through the hole in the left diaphragm. All of the small intestines but about 2 in. from the pylorus to the hole in the diaphragm are contained in the chest cavity as well as the appendix and colon, except for the descending colon, which is in its usual position. The mesentery is attached in the usual way, but seems to be considerably stretched. The intestines can be readily pulled back into the abdomen through the hole in the diaphragm.

CASE IV. (From Knickerbocker Hospital.)

November, 1920. P. D., aged forty-three, blacksmith.

Previous History. This yields no information other than the usual diseases of childhood and erysipelas.

Present Illness. Dates back to the day before admission. He had been performing his daily work when he was seized with vertigo and experienced severe pain in the epigastrium and lower left chest which pain also radiated upwards to the left clavicle. The pain was exaggerated by deep inspiration and he had to confine himself to short respirations. A cough which he has had for the past seven years has become much more aggravated. He had also complained of dyspnea on exertion for the past seven years. Since admission he has been vomiting a dark brown material constantly and there is marked dyspnea and cyanosis with a very feeble and rapid pulse. There was no history of injury.

Physical Findings.

Chest: There was a definite bulging of the lower left chest posteriorly with a distinct limitation of motion. Resonance was present throughout except over the lower third of the left chest anteriorly where tympany was elicited. The breath sounds were harsh throughout and absent over the lower third of the left chest posteriorly where succussion sounds were heard.

Abdomen: In the abdomen there was distinct rigidity over the right upper quadrant and tenderness over the epigastrium where a hard palpable contracting mass was also felt.

Autopsy (Dr. Hohman).

Body that of a well developed male showing no external abnormalities except for a barrel-shaped chest, abdomen "normally" distended.

Usual median line incision was made thereby exposing thoracic and abdominal contents.

Thorax: Right lung firmly adherent on all surfaces, pleura markedly thickened. Right lung very firm from extensive fibrosis due to an existing fibroid tuberculosis.

Left lung compressed to one-third its natural size showing a pathological condition similar to the right—also adherent and fixed to the chest wall, except at the base, which is decidedly concave from contact with the curvature of the stomach.

The remainder of the thoracic space was occupied by an enormously dilated stomach filled with blood stained fluid, and the spleen which was adherent to the stomach. A portion of omentum was firmly adherent to the 5th interspace in the axillary line.

The left dome of the diaphragm was perforated—contained a 3½ in. hernial ring—no sac—the margin of the ring was thickened from fusion of the pleura and peritoneum—the hernial ring contained the entire splenic flexure of the colon together with the first and second portions of the duodenum, both of which together with the stomach showed gangrenous changes from circulatory obstruction.

The heart instead of obliquely lying in the chest was vertical, producing a wrinkling of the aortic arch 1½ in. from its orifice.

Liver, spleen and kidneys showed extensive fibrosis from alcoholism.

Intestinal tract congested throughout.

Bladder partially filled with urine—mucosa normal.

Prostate and pancreas apparently normal.

Vascular system showed a moderate sclerosis.

Cause of Death: Strangulated stomach and intestine in diaphragmatic hernia with bilateral pulmonary tuberculosis.

CASE V.

From the Service of Dr. Knipe of Gouveneur Hospital—was a new-born infant. The physical signs, roentgen findings and autopsy examination were all exact duplication of Case I.

CASE VI (From Bellevue Hospital.)

June 17, 1918, J. P., male, aged thirty-six, salesman.

The previous history of this patient was unobtainable but he was removed by ambulance from a railroad station where he had been and was seized with sudden severe abdominal pain and vomiting of blood. He expired shortly after admission.

Autopsy (Dr. Schwartz).

Anatomical Diagnosis. Congenital diaphragmatic hernia with volvulus and strangulation of small intestine and the transverse and descending colon; dilatation of stomach; compression atelectasis of entire left lung; congestion of right lung; arrested development of spleen with compression; malformation of liver (mechanical); anemia of viscera, and extensive stasis with hemorrhagic infiltration of intestine with free blood in the lumen.

Body is that of a well-developed white male, 5 ft. 5¾ in. in height, about thirty-five years old and weighing about 150 pounds. *Rigor mortis* is absent. There is a slight amount of post mortem discoloration of the skin of the

back. Hair on head is black, thick and abundant. On the face the hair is abundant and equally distributed. Axillary and pubic hair is normal in amount. No scars or pigmentation and no evidence of trauma on the body surface. Pupils are in mid-dilation and equal. The conjunctival sacs and sclerae are clear. There is a slight mucoid discharge from both nostrils. The teeth and gums are well preserved. The oral mucosa is almost white from pallor. The chest is symmetrical and normal in shape. The abdomen is somewhat distended. Extremities are normal. Over the entire left chest both anteriorly and posteriorly the percussion note is distinctly tympanitic. Section reveals a moderate amount of panniculus adiposis which measures ¾ inch thick at the level of the umbilicus. The intestines are distended with gas, the walls are of a deep red color showing marked hemorrhagic infiltration. The appendix is located at the ileocecal junction about one inch above and to the right of the umbilicus. The diaphragm on the right side is at the level of the fifth rib. On the left side it is depressed to the level of the seventh space and here the hand sinks into a perforation of the diaphragm into the chest cavity. On exposing the chest, the left pulmonic cavity is seen to be completely occupied by coils of intestines and stomach, which upon examination reveal almost the entire jejunum, the proximal ⅔ of the ileum, the entire transverse colon, the major portion of the descending colon, and the entire stomach from the cardia to the pylorus. The pyloroduodenal junction is still bound down in the abdominal cavity in its normal location and is under some tension. The heart is completely dislocated to the right of the median line so that the apex corresponds to a point on the surface one inch below and a half inch to the right of the right nipple. There is almost total compression atelectasis of the left lung.

Lungs: The right pleural cavity is free from adhesions. There is a small amount of blood tinged fluid posteriorly. The surface of the right lung is deeply congested, especially in the region corresponding to the area of compression by the heart. On section there is an increased amount of blood, but the lungs crepitate, float in water and are free from changes. The left lung consists, as normally, of two lobes, the entire structure removed close to the primary bronchus weighs seven ounces, and is completely compressed beneath the left clavicle to the extreme superior extremity of the left apex.

The size corresponds to ¾ dimensions of a fist. The lung substance is grayish white from pallor, slightly crepitant, very elastic and almost bloodless. There is normal ramification of the bronchi. Sections float in water.

Heart is completely dislocated to the right of the median line. The precordial area is normal in size and encroached upon by a portion of the middle lobe of the right lung. The pericardial cavity is free from fluid and adhesions. The epicardium presents no hemorrhages. The myocardium is pale brown in color and of normal consistence. The cavity of the left ventricle is very firmly contracted so that the left ventricle (cut in transverse section) presents a mere slit in the position corresponding to the location of its cavity. The endocardium is perfectly smooth and glistening. All the valves are competent. No hemorrhages. The thoracic and abdominal aortae are of normal elasticity and there is no evidence of atheroma or other changes.

Diaphragm: The right side is normal. On the left side the dome of the diaphragm gives rise to an almost perfectly circular deficiency with a diameter of 7½ inches. The boundary of this deficiency is perfectly smooth, pale, almost fibrous, and free from any evidence of laceration with a total absence of any hemorrhage in this vicinity except for the blood oozing from the intestines as a result of venous stasis. In addition to the structures described above as passing through the aperture, there is now seen a process of the left lobe of the liver soon to be described.

Liver: Extends one finger beneath the right costal margin. A tongue shaped process of the left lobe projects through the aperture of the diaphragm into the left chest. The liver tissue corresponding to the zone of compression by the fibrous band is pale, hollowed out and compressed. The capsule is normal. The substance cuts with normal resistance. The lobules are normally arranged and the liver substance is very pale. Gall-bladder is distended with greenish, viscid bile and empties readily on pressure. Ducts are patent.

Spleen is dislocated posteriorly, firmly adherent to the under surface of what remains of the left portion of the dome of the diaphragm. On removal it is seen to be almost infantile in size, the dimensions being 4 cm. transversely by 2.5 cm. longitudinally by 1.5 cm. thick. The surface is slate gray in color and on section the splenic substance immediately beneath the capsule on the diaphragmatic surface is bluish from congestion and compression while the substance away from this grows gradually pale. The Malpighian bodies apparently increased in number, are firmly compressed and closer to each other than normal. The notches are normal.

Pancreas is normal in size and shape. On section the lobulations are normal. The cut surface is extremely pale.

Gastrointestinal Tract: The mucosa of the esophagus is deeply engorged. The stomach is located in the left chest cavity and twisted once on its longitudinal axis at the level of the pylorus. It is tremendously dilated and the transverse diameter in its center is 18 cm. On section there escapes about one quart of bloody, sour-smelling material. The entire jejunum, and the proximal ¾ of the ileum in the chest cavity, are markedly distended and strangulated at the point where they are constricted by the fibrous band in the diaphragm. Several of the intestinal coils are several times twisted on their longitudinal axis and the walls of the intestines show marked hemorrhagic infiltration. They are extremely friable and in places almost necrotic, particularly on either side immediately above and below the zone of strangulation. The lumen contains a large amount of bloody fluid.

Adrenals are normal in size and present a rather narrow cortex and pale medulla. No gross lesions.

Kidneys are normal in size and imbedded in a normal amount of perirenal fat. The capsules strip readily and expose a smooth, rather pale cortex. On section the markings are distinct and the cortex and medulla normally related to each other. Cut surface is extremely pale. Pelves and ureters normal. The bladder contains a small amount of turbid fluid. Trabeculation is normal. The mucosa is rather pale.

Testicles are normal in size and consistency, the color pale brown. The tubules pull out readily. There is a hydrocele on the right side.

Case vii. Mrs. F. K., aged forty-eight, Case of Dr. A. E. Sellenings.

Patient is an adult female, white, of slight frame and weighs about 100 pounds. Has never had any serious illnesses and has only had medical attention at times of pregnancy, of which there were four. Nineteen and a half years ago gave birth to a seven months old dead fetus. Her oldest child is twenty-four, her second twenty-two and her youngest is eighteen. All the children are strong and healthy. On October 18, 1922, while crossing the street was struck by a taxicab and sustained an injury to her left humerus. It was as a result of roentgen examination that the diaphragmatic hernia was discovered for she presents no other symptoms at all.

The roentgen report is as follows:

The left shoulder (stereoscopically) compared with the right:

The humerus: The upper 4 inches of the shaft shows a spiral fracture with an oblique fracture at the surgical neck where there is about ¼ inch over-riding and estimated ¼ inch anterior and ½ inch internal displacement with apparently no impaction.

The ribs in this region show no evidence of any fracture.

The chest (stereoscopically):

The left lung is entirely collapsed, except possibly a small area the size of a half dollar in the region of the apex. This is evidently a very old condition, since the ribs in this region are deformed, the mediastinum displaced 2 inches to the left by the compensatory emphysema on the right. There are several calcified glands in the region of the upper part of the left chest and a general appearance of fibrosis. This with the general shape of the chest and lack of expansion argues that this is a very old condition.

The lower two-thirds of the chest communicating with the abdomen is taken up with a large collection of air or gas which is divided into regular segments such as the colon would be; and the shadow is probably that of the colon which has been displaced about 8 inches into the chest through a hernia of the diaphragm for probably many years. There is no evidence of any fracture of any of the ribs to suggest a puncture of the lung and no evidence of any diaphragm. In fact there is nothing to indicate that this is a recent condition. Whether this is the colon or not can be definitely proven by giving the patient a barium meal and taking roentgen plates twenty-four hours after. The stomach is probably also in the lower part of the chest.

The right lung: The root to all lobes shows a peribronchial thickening and fibrosis with occasional parenchymatous infiltration suggesting an old chronic inflammatory condition very suspicious of tuberculosis.

The patient has refused to submit to further roentgen study, such as a gastrointestinal series.

DIFFERENTIATION OF EVENTRATION AND DIAPHRAGMATIC HERNIA BY ROENTGEN RAYS

The differentiation of eventration from diaphragmatic hernia can surely and positively be made by means of the roentgen ray, especially under roentgenoscopic examination. In eventration we see the dome of the diaphragm apparently pushed into the chest cavity, compressing the lungs and displacing the heart. The diaphragmatic dome may even reach the level of the 2nd and 3rd intercostal spaces and it is

perfectly regular in outline and shows no defect and moves evenly with respiration. A bismuth injection of the viscera shows the entire abdominal contents below the dome of the diaphragm or in other words, retained in the abdominal cavity.

PROGNOSIS

We can consider three classes of cases. In the first class we have those who die at birth or shortly afterwards. Statistics (Bowditch) show that nearly half of these never breathe nor can be made to breathe. They die at the moment of birth for although the placenta and its circulation may be perfect and the infant apparently well formed except for the deficiency in the diaphragm, he cannot inspire and dies instantly after a gasp or two. There may be some very feeble attempts at crying and for a very short time he apparently rallies but his doom is sealed, for in a very few hours there is a relapse followed by death. In some of these cases the sympathetic action of the central nervous system comes into play and the scene is closed by a convulsion.

In the second class the child lives for a few months, or even a few years but in a condition of impaired health. Dyspnea is the most common symptom and is very easily brought forth by the slightest exertion. There is a chronic difficulty or embarrassment of respiration and the patient usually expires in a few months to a few years.

The third class deals with the adult. Notwithstanding the marked mal-development of the diaphragm the patient may be able to perform any hard work. Though apparently generally healthy, these individuals may complain of mild dyspnea and vague gastric manifestations and following a sudden severe strain they go into shock and present the picture of a strangulation or cardiac failure and they expire. Other patients give no symptoms whatsoever and live on in perfect health, the hernia being demonstrable accidentally when the abdomen is opened for some surgical procedure or when the patient dies and an autopsy is performed, the cause of death being separate and distinct from the thoracic conditions. It may be interesting to note the last case of congenital diaphragmatic hernia which had accidentally been discovered when a roentgen examination had been taken for a fracture of the humerus and a part of the chest was included. Such cases may go on and die from something entirely remote from their congenital hernia.

We wish to thank Dr. Norris for the courtesy of the autopsy reports; also Dr. Knipe, Dr. Sellenings and Dr. Schwartz.

PYELITIS IN PREGNANCY*

BY P. F. BUTLER, M.D.

From the Francis H. Williams Roentgen Ray Laboratory, Boston City Hospital

BOSTON, MASSACHUSETTS

URINE analysis for determining the presence of disease in the urinary tract is admittedly subject to wide variations of error and is not dependable in many cases. One kidney may have complete loss of function while the other kidney is secreting normally, or there may be various anomalies of the kidneys and ureters which cause subjective symptoms and still show a normal urine. Many times one specimen will be normal while a later one will show definite evidence of disease.

Study of the urinary tract by the injection method, on the other hand, is far more accurate, for it not only demonstrates the presence of pathology but it often shows the anatomical extent of the lesion. It is especially adaptable to cases of pyelitis in pregnancy because in these cases the treatment consists of drainage and lavage and this is accomplished at the same time that the diagnostic study is made. Of course the study of the urine both chemically and bacteriologically must be carried on at the same time, as it still has an important place in diagnosis.

FIG. 1. Three months pregnant. Old hydronephrosis with dilated ureter; catheter relief.

FIG. 2. Three months pregnant. Bilateral hydronephrosis with acute attack.

For about two years we have been routinely examining our cases of pyelitis in pregnant women by this method. Many interesting and instructive facts have been determined. The infecting agent has been found most frequently to be the colon bacillus but occasionally staphylococci and streptococci have been found. The condition has been found most often in multiparas. It may occur early or late in the pregnancy. When one side is affected it is usually the right side (80 per cent in our experience). This right-sided frequency

*Read at the Twenty-sixth Annual Meeting, AMERICAN ROENTGEN RAY SOCIETY, Washington, D. C., Sept. 22–25, 1925.

was thought to be due to the frequency of right-sided head presentations but many cases develop the condition too early in pregnancy for such pressure to be an etiologic factor. It may be due to the proximity of this ureter and kidney to the cecum and ascending colon and because of the intimate association of their lymph channels. The ascending colon and right kidney are much more movable and liable to prolapse than the corresponding organs on the left, and because of this fact they may be brought into closer proximity; are not blocked by pus, mucus, fetal pressure or edema in the ureter. Plugging of the ureter, followed by absorption of toxins may give the typical symptoms of severe sepsis. Pain may be absent, especially when there is no obstruction in the ureter. There is usually frequent urination, which may or may not be painful. The pain is usually located in the back. The symptoms generally clear up after delivery.

The diagnosis is first made by careful and frequent examination of the urine, plus the history. Pus and colon bacilli

FIG. 3. Four months pregnant. Dilated pelvis and ureter; catheter relief.

FIG. 4. Five months pregnant. Pelvis dilated and ureter kinked; catheter relief.

this is an important consideration in the presence of pathology on the right side in any of these organs. Low fluid intake and lowered resistance also are undoubtedly factors in causing the condition. Fetal pressure is the cause in some instances but probably in the minority of them. Primary pyelitis occurs in some of the cases but the general belief is that there has been a previous renal or ureteral infection and that the abnormal conditions have lit up the old pathological process.

The symptoms depend upon obstruction of ureter or severity of infection. There may be no symptoms when the ureters are both found as a rule. When the foregoing picture is presented injection study is indicated. The condition may be confused with appendicitis, gall-bladder pathology or pelvic inflammation, but urine study and pyelography serve to differentiate.

The treatment is simple; plenty of water, rest and renal lavage. Simple catheterization of the ureters generally clears up the condition. Plain sterile water or some simple antiseptic solution is all that is necessary for the lavage, if it is needed. It is well also to leave the catheters in position for an hour or more after the lavage, to provide ample drainage. Most

of our cases recovered after simple catheterization of the ureters without lavage.

Injection of the urinary tract in pregnant women does not present any special difficulty. Sometimes the bladder is distorted by pressure from above but the exercise of a little patience will soon locate the ureteral orifices. Sometimes the catheter is arrested in the ureter by uterine pressure but this difficulty is not common and generally the solution can be forced beyond the pressure point. It is unsafe to attempt to force the catheter past an obstruction. A ureteral kink, if not permanent, may easily be straightened out by the catheter while if it is permanent it will usually allow passage of the solution. Sometimes a catheter will curl up in the bladder or dilated ureter and deceive one as to the distance it has entered the ureter. For some time it was deemed inadvisable to inject both sides at one sitting, but with the use of sodium iodide solution there is practically no danger of suppression or kidney tissue injury. It is a wise precaution, however, to allow the catheters to remain in the ureter for a few minutes so as to obtain complete drainage of the solution.

The patient is prepared for examination by taking six ounces of mineral oil at six o'clock on the preceding evening and omitting supper and breakfast. This cleans the bowel thoroughly and does not result in paresis and dilatation of bowel with gas, as many other cathartics do. The injection solution should be warmed slightly to avoid spasm, which is often due to the use of a cold solution. The patient should be placed in a comfortable position during the procedure so as to prevent cramping of muscles. Selection of the proper sized catheters and cystoscope is essential for facilitating the work. Good illumination of the bladder obviates unnecessary trauma and pain in locating the ureteral orifices. In other words, a competent and properly equipped urologist only should do this part of the work. A Potter-Bucky diaphragm is essential and the entire examination should be made with the patient in position on the diaphragm. A further refinement may be added by taking the films with the patient in the sitting position, although this is not

FIG. 5. Six months pregnant. Dilated pelvis and ureter; fetal pressure; catheter relief.

FIG. 6. Six months pregnant. Perinephritic abscess; distended ureter and pelvis; normal delivery at eight months, four weeks after perirenal drainage.

essential. Routinely four large films are made, one after the first kidney is injected, the second when the catheter has been withdrawn to the level of mid-sacrum, the third after the second kidney is filled and the fourth when the second catheter has been withdrawn to the same level. The ureter must be injected as the catheter is being withdrawn.

These pyelitis cases may be divided into three types anatomically: (1) Simple dilatation of the ureter and renal pelvis with or without kinks in the ureters; (2) dilatation of the renal pelvis with blunting of the calyces from continued infection and increased pressure, and (3) real destruction of the kidney substance. The first type is apparently very common; a study of a series of cases with no subjective symptoms and normal urinary finding has revealed a large percentage of dilated ureters and pelves. Some observers feel that no significance should be attached to these cases, while others feel that they should be watched very carefully to prevent infection resulting in a more advanced lesion with permanent crippling of the ureter and destruction of the kidney. There can be no doubt that a hydronephrosis, with its resultant stagnant urine offers an excellent field for infection. Many of our cases were of this type but had pain and pus in the urine. Catheterization of the ureters and drainage of the ureters and pelvis relieved all of these cases for months, and they practically all cleared up after delivery. The second type with the blunting of the calyces from continued pressure usually are complicated by plugs and mucus. Drainage with lavage of the renal pelvis may have to be repeated once or twice. Hexamethylenamine may be of assistance. When there is real destruction of the kidney substance the symptoms are usually very severe and the condition does not clear up after pregnancy. In one of the first cases of this series complete destruction of the kidney occurred with the formation of a perirenal abscess, deep sepsis and death. In cases of this type it might be wise to remove the diseased kidney after delivery of the patient.

FIG. 7. Seven months pregnant. Chronic pyelonephritis with acute exacerbation; miscarriage; nephrectomy four weeks post partum.

FIG. 8. Two weeks post partum. Old kink in ureter; mild pyelitis; catheter relief.

SUMMARY

1. Deformities and infections of the urinary tract in pregnant women are easy to diagnose.

2. Frequent study of the urine gives the first clue to these conditions. Subjective symptoms develop later; these demand careful investigation and early treatment.

3. The treatment is very simple and effective; catheterization alone usually suffices.

4. Careful prenatal study of cases will disclose the disease early.

5. Cooperation between the roentgenologist and urologist reveals the entire picture.

DISCUSSION

Dr. John T. Williams, Boston. Speaking from the point of view of the clinical obstetrician, I want to say that the addition of the pyelogram as a diagnostic method in the pyelitis of pregnancy as described by Dr. Butler has been of great value. I should like to emphasize five points in his paper.

First: Accuracy of Diagnosis. No other single diagnostic means gives us quite the same accurate picture of the pathology present as does the pyelogram. It has shown us that we must divide the cases of pyelitis during pregnancy into two classes. First: those which are merely the lighting up of an inflammatory process in an old hydronephrosis of greater or less degree, and second, those which are really acute primary pyelitis of pregnancy, an infection arising in a kidney where there is only a temporary dilatation of the ureter and kidney pelvis from pressure of the fetal head.

A careful analysis of the pyelograms which have been exhibited shows a large preponderance of cases of the former type. The only other observer who has done work of importance on this subject is Kretschmer of Chicago. He has shown that dilatation of the kidney pelvis is very frequent during the latter months of pregnancy without infection. Kretschmer believes that in nearly all cases of pyelitis during pregnancy the dilatation of the kidney pelvis is due entirely to the pregnancy and will clear up after delivery. While our observations agree with his in a certain number of instances, the blunting of the calyces, the kinking of the ureters and the extreme dilatation of the kidney pelves as shown in the pyelograms in the majority of our cases point to a pre-existing process aggravated by the increase in pressure during pregnancy. Whichever pathology may be present in a given case will be demonstrated by a pyelogram and an accurate picture of the lesion obtained.

The second point which I wish to emphasize is the *harmlessness* of this procedure. Not a single unfavorable reaction occurred after the pyelographies in this group. The pain was transient and quickly disappeared after completion of the examination. In several cases the pyelogram was taken while the inflammation was in a fairly acute stage, a few patients even having some rise in temperature.

The third point is *the therapeutic value of ureteral catheterization in these cases.* Every case improved after ureteral catheterization due to the reestablishment of drainage. Lavage of the renal pelvis was not done in any case in this series and seems to be unnecessary. The catheter may be left in the ureter from one hour to several days without harm. In very acute cases of pyelitis it would be better perhaps to carry out a preliminary ureteral catheterization for drainage, to be followed after subsidence of the acute symptoms by the pyelography.

A fourth point of importance is that *drainage of the renal pelvis by the ureteral catheter has made therapeutic abortion unnecessary* to relieve pressure on the ureter. At the Boston City Hospital no induction of labor for pyelitis during pregnancy has been done for several years.

The fifth and last point which I would emphasize is the *technique of cystoscopy during the latter months of pregnancy.* The ureters are often somewhat displaced as the uterus enlarges rendering their identification difficult and sometimes catheterization impossible. After the fetal head has entered the pelvis catheterization of the ureters should not be attempted.

COMPLETE BILATERAL DUPLICATION OF URETERS AND RENAL PELVES

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THE development of cystoscopy and pyelography has made it possible to diagnose and study many of the anomalies of the kidneys and ureters formerly undiscovered until operation or autopsy.

Braasch, with the wealth of material at his hands, has made a complete study of these conditions, and concludes that duplication of ureters is practically always found with double renal pelves, these latter surrounded by separate or fused kidneys.

According to the statistics of Harpster, Brown, and Delcher, Geiringer and Campuzano a thorough study of the literature shows 181 cases of complete unilateral duplication, 133 cases of incomplete unilateral duplication, with only 40 cases of complete bilateral duplication. A detailed study of the 40 cases reported of complete bilateral duplication shows that 14 were discovered at autopsy, 17 at operation, while only 9 were diagnosed by cystoscopy and pyelography.

Owing to the comparatively few cases of this condition diagnosed before operation or autopsy the following case is reported.

FIG. 1. Right side injected with sodium iodide solution, showing double ureters and pelves.

FIG. 2. Left side injected with sodium iodide solution, showing double ureters and pelves with four catheters in place.

Miss N. H., white, aged nineteen, referred by Dr. W. B. Porter.

Past history negative.

Present History: Has been complaining of vesical irritation for several months, which was not relieved by medical treatment. Patient well nourished, and otherwise in good health. Urological examination reported by Dr. Cary as follows:

Bladder: Moderate trigone congestion.

Urine from bladder slightly cloudy, 1010, acid reaction, albumen and sugar negative. Pus, 2 plus.

Cystoscopy: Right ureteral cornu showed two openings—about half an inch apart, both normal in appearance. Catheters introduced into both openings and passed up to the kidney. Separate specimens collected for examination. Urine pale and clear in both specimens. Microscopic examination and culture of both specimens negative.

Left ureteral cornu showed two openings—about half an inch apart, both normal in appearance. Catheters introduced into both openings and passed up to the kidney without meeting with resistance. Separate specimens collected for examination. Urine pale and clear in both specimens. Microscopic examination and culture of both specimens negative.

Three to 4 c.c. of sodium iodide solution was injected into both catheters on each side.

Roentgen examination of urinary tract showed the presence of bilateral, double ureters, the right side showing one of the ureters crossing the other ureter twice, the course otherwise being normal. Injection of the right side with sodium iodide solution showed the presence of two definite, distinct pelves.

The left side showed the presence of double ureters, running parallel, side by side, there being also a double pelvis on the left side, demonstrated by injecting sodium iodide solution. No abnormalities were noted in the course of the left double ureters.

Dr. Cary's conclusions were that the congenital condition did not play a part in the symptoms complained of, the cystitis being the only pathological condition found. Bladder irrigations were suggested, and the patient's vesical symptoms improved.

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TUBERCULOSIS OF THE SACROILIAC JOINT

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CONSIDERATION of tuberculous disease of the sacroiliac joint has not been ignored although relatively little seems to have been written of it in recent years. No statistics are available concerning the frequency of the condition, but in comparison with tuberculosis of the hip-joint and spine it is referred to by authorities as being uncommon or rare. Ridlon[1] states that there are very few cases of sacroiliac tuberculosis, probably not one to a hundred of tuberculous hip. Inquiry of a number of roentgenologists of wide experience shows that 4 of these cases is the average number seen during the past ten years. It is most frequently found in young adults and seems to be extremely rare in children.

Although it has been known for many years that a certain amount of motion takes place in the normal sacroiliac joint and that a physiological increase in the mobility of the joints occurs during pregnancy, it appears that no particular importance was given to the consideration of the anatomical structure and the pathological conditions involving the joint prior to the studies of Goldthwait and Osgood,[2] in 1905.

Albee[3] in 1909 emphasized the fact that the sacroiliac articulation is a true joint, having all the common joint structures and being subject to the same diseases and injuries as other joints.

ANATOMY

The sacroiliac joint is a diarthrosis formed by the opposing auricular surfaces of the sacrum and ilium. These surfaces are slightly irregular and more or less

completely covered by hyaline cartilage, the resulting joint space being very narrow.[4]

The sacrum acts as the keystone of an arch between the innominate bones and is wider anteriorly as well as at the top. In the erect posture the normal forward tilt of the sacrum is increased, so that the anterior surface really faces downward and the keystone is inverted.

The ligaments forming the anterior capsule of the joint are thin but the posterior ligaments are very strong and suspend the sacrum and the weight of the superimposed trunk from the innominate bones. Practically all the mechanical stresses produced during the acts of moving or carrying heavy objects are transmitted to this posterior group of ligaments.

Considering the anatomical structure of the joints, it is remarkable that they are not more frequently affected by disease and injury for, unlike other joints, practically no bony contact is provided to relieve the strain on the ligaments when subjected to the stress of weight-bearing.

The proximity of the lumbosacral cord, which is formed by the junction of the fourth and fifth lumbar roots with the first and second sacral roots over the upper part of the anterior surface of the joint, has special clinical significance and explains the frequency of pain in the region of distribution of the sciatic nerve.[5]

PATHOLOGY

Tuberculosis produces the same changes in the sacroiliac as in other joints. The disease is seldom bilateral and usually begins in the sacrum or ilium, more frequently in the former, to which it may have extended from a focus in the lumbosacral joint.

Bone destruction occurring with secondary extension to the joint may be arrested at an early stage with resultant obliteration of the joint, caries sicca. More often perhaps there is destruction of the joint surfaces with perforation of the capsule and the formation of the so-called cold abscess, more properly designated as an ichor pocket. The perforation usually occurs anteriorly through the weakest portion of the capsule into the pelvis, from which the abscess may extend through the greater or lesser sacro-sciatic notch upward along the posterior aspect of the joint into the gluteal region. However, it may point in the groin or the ischiorectal fossa, or rupture into the rectum.

SYMPTOMS AND PHYSICAL SIGNS

(1) Pain occurs early and is usually unilateral whether localized to the joint region or referred to areas supplied by the sciatic nerve. Any motion which increases the strain on the joint will aggravate the pain, which is relieved by postural changes decreasing the strain. The pain may disappear after rupture of the joint capsule.

Tenderness which is frequently noted on direct pressure over the joint is not present in sciatic neuritis. Nuttall[6] considers this the most reliable sign in the early stages. A further differential point between these conditions is found in the fact that pain is not increased by pressure along the course of the nerve as in sciatica. Lateral compression of the pelvis usually produces pain on the affected side.

(2) Limitation of motion is due to the voluntary restriction of those motions of the lower back which produce pain by increasing strain on the sacroiliac joints.

With the patient seated, forward bending is not especially limited as in lumbosacral disorders, although this motion is markedly limited when the patient stands because of the leverage exerted on the pelvis by the hamstring muscles.

Smith-Petersen[7] finds that passive flexion of the lumbar spine is of particular value in differentiating sacroiliac and lumbosacral disorders. If the examiner flex the thighs of the supine patient he will note good flexibility of the lumbar spine in sacroiliac cases but the lumbar spine remains fixed, and flexion of the hips is possible through a very limited arc, if the lesion is in the lumbosacral region.

Raising of the leg with the knee joint extended is definitely limited, as stretching of the hamstring muscles, which are attached to the ischia, brings the sacroiliac joint into play. Further flexion of the thigh causes pain referred to the sacral region or legs (Goldthwait sign).

(3) Peculiar attitudes in standing, sitting, and walking include the inclination

of the body toward the sound joint, standing with the weight on the unaffected leg, taking short steps when walking and the dragging of the affected leg while climbing steps.

(4) Swelling due to infiltration of periarticular structures may appear fairly early but is not especially characteristic. Later rupture occurs through the weak anterior portion of the joint capsule into the pelvis with abscess formation which may be detected by rectal examination.

(5) Feeling of weakness or insecurity of the back.

Some of these findings are present in other types of sacroiliac disease so that reliance must be placed on the history, clinical course and roentgenological examination to eliminate the confusing factors.

Anatomical variation is the basis of certain pathological conditions which must be carefully considered in the study of any case having symptoms referable to the lower back. These include:

(1) Abnormal relations of fifth lumbar vertebra and sacrum.

(2) Differences in planes of articulating facets between the fifth lumbar vertebra and the sacrum[8] permitting unequal rotation.

(3) Anatomical defects in the neural arch of the fifth lumbar vertebra.[9]

(4) True spondylolisthesis which may be due to any of the above changes when associated with relaxation of the posterior ligaments.

(5) Abnormally long or broad transverse processes of the fifth lumbar which actually impinge on the wing of the ilium or sacrum, perhaps with the formation of a joint which becomes diseased.

(6) Calcification of the ligaments[10] extending from the transverse process of the last lumbar to the ilium.

Among the lesions which may be confusing in the differential study are included:

A. Those affecting the sacroiliac joint.

(1) Arthritis, which may be of pyogenic origin or due to typhoid fever, gonorrhea, puerperal sepsis or osteoarthritis.

(2) Relaxation.

(3) Actual injury as in strain or subluxation.

(4) Malignant disease.

B. Those affecting neighboring structures.

(1) Tuberculosis of the hip.

(2) Tuberculosis of the lumbar spine.

(3) Sciatica.

(4) Infectious and malignant disease of the adjacent bones.

(5) Traumatic sprain of lower back not involving the sacroiliac joint.

(6) Arthritis of the spine.

(7) Disease or displacement of the pelvic organs or defective posture producing backache.[11]

Roentgenological examination of the lower back is of the utmost importance as many of these confusing factors may be ruled out through negative findings. Positive findings are dependent on destructive bone changes and should be found relatively early. Phemister,[12] in speaking of joint tuberculosis, states that "when the lesion is primary in the bone a localized area of reduced bone density appears *early* as a result of bone destruction." In the *early* stages of the disease, according to Smith-Petersen, increased density is found along the joint line and in the soft tissues of the inferior margin of the joint.

If roentgen examinations of suspected cases were made at frequent intervals (every two weeks) the percentage of early positive diagnoses would, no doubt, be markedly increased.

The absence of the history of trauma together with the insidious course of the disease and clinical findings, which are only moderately severe, should point the way to the diagnosis.

Probably the major difficulty will be encountered in the differentiation of tuberculosis from the other affections of the sacroiliac joint.[13]

The more acute types of infectious arthritis give a more acute symptomatology with acuteness of onset, elevation of temperature and redness in the region of the joint, probable involvement of other joints and more rapid joint destruction which can be demonstrated roentgenologically. Typhoid, gonorrhea, and puerperal sepsis may be reasonably ruled out by a negative history with negative physical and laboratory findings. Hypertrophic changes are found in osteoarthritis.

Direct inspection of the joint surfaces and microscopic study of excised tissue is not always possible, so that the differentiation must often rest on the clinical and roentgenological findings. The appearance of a fluctuating mass and the roentgen study of the case should render the diagnosis conclusive.

ness have disappeared, and then a cast on the body and well leg. He states further that motion at the well hip joint strains the diseased sacroiliac joint more than motion of the hip joint on the diseased side.

Before abscess formation the joint may be ankylosed by the operation devised by

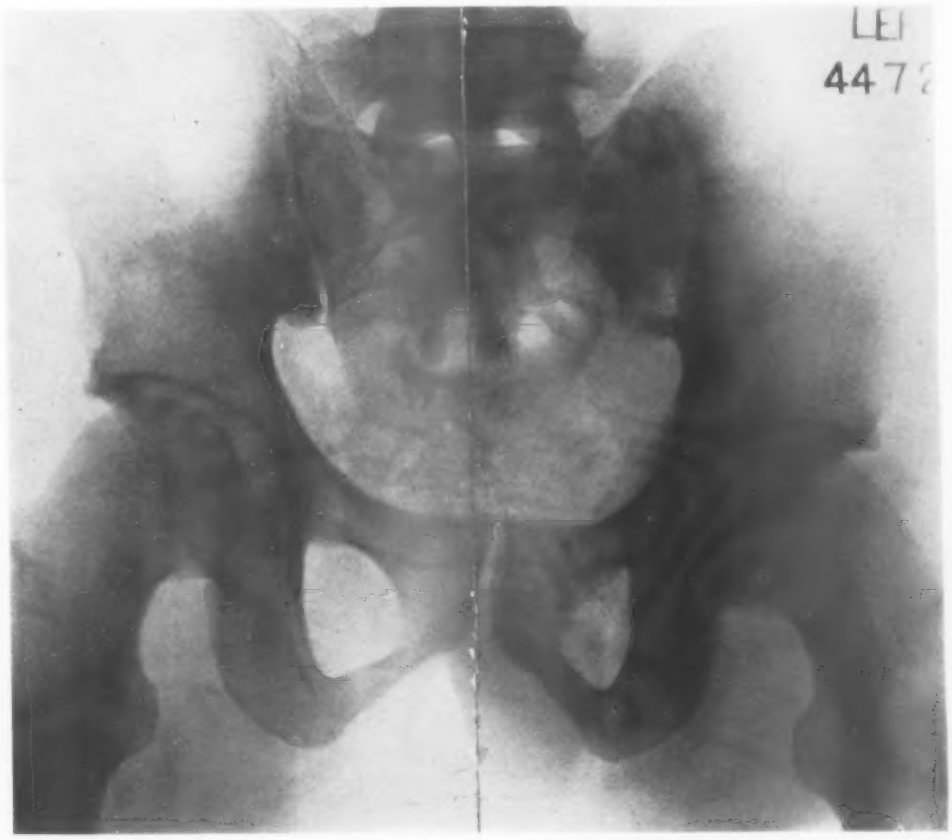

FIG. 1. Tuberculosis of the left sacroiliac joint.

TREATMENT

Therapeutic measures should follow the accepted procedures which have been found most valuable in the treatment of other joints similarly affected. The disease is one of marked chronicity requiring treatment over considerable periods of time and offers an unfavorable prognosis.

The diseased joint should be protected from further injury by suitable brace or plaster cast. Ridlon advises the application of a plaster cast including the body and both legs until all pain and sensitive-

Smith-Petersen or fixed by placing a bone graft across the joint after the manner of Albee. Abscess over the posterior aspect of the joint should be treated by surgical incision, removal of the diseased structures and drainage. Pelvic abscess should receive direct drainage to prevent burrowing.

CASE REPORT

E. R. R., laborer. Admitted to Hospital Feb. 2, 1925.

Adult, male, colored, aged thirty-eight.

Past history negative. Denies venereal infection.

Marital history, wife living and well, no miscarriages. Two children living and well.

Chief Complaint: Swelling and weakness of lower back.

History. About eight months prior to admission to the hospital, patient began to have pain of moderate severity in left hip region. Thought he had "rheumatism." The pain increased in severity and at times extended into the thigh and leg. About six weeks later, a small lump appeared mesial to the upper part of the left buttock. At this time the pain ceased and the disability became less marked. As the mass slowly increased in size, the patient noted that there was a feeling of weakness in the lower back which became progressively worse. He attempted work in September but could not do so because of weakness (without particular discomfort) of lower back.

There were no symptoms referable to the cardiorespiratory, genitourinary or gastrointestinal systems. Appetite always fine. Thinks he has lost weight.

Physical Examination. The general physical examination is essentially negative with the exception of the findings referable to the lower back. The patient stands with the weight thrown on the right leg. Forward bending of the lower back is not restricted.

Passive flexion of the left thigh is not limited nor does it produce pain in the lower back.

Two inches below the left iliac crest posteriorly, there is a large rounded mass as large as half a grape fruit. The mass measures about five inches in vertical and lateral diameters, and fluctuates on pressure.

There is no tenderness on direct pressure over the sacroiliac joint posteriorly or along the sciatic nerve.

Lateral compression of the pelvis produces no pain.

Rectal examination reveals no significant findings.

Examination of urine and blood, including Wassermann reaction, are negative.

Roentgenological Examination. The study of the pelvis and lumbar spine shows the right iliac crest slightly higher than the left and the lumbar spine slightly tilted to the right. These findings are probably due in part to inability to place the patient symmetrically over the film because of the large swelling above the left buttock.

There is no narrowing of the intervertebral spaces or deformation of the bodies of the vertebrae.

The right transverse process of the fifth lumbar vertebra is of the broad, so-called sacralized type and apparently articulates with the upper surface of the sacrum but not with the wing of the ilium.

The right sacroiliac joint is apparently normal.

The left sacroiliac joint shows increased width and decreased sharpness of outline of the joint space. In the upper two-thirds, the joint margins are of increased density; while in the lower third, there is an area of decreased bone density about 2.5 cm. in diameter. The central portion of this area, which is in the ilium, shows complete absence of bone detail. The surface of the opposing sacral portion of the joint is irregular.

The study indicates an area of bone destruction involving that portion of the left ilium which is contiguous with the lower third of the sacroiliac joint, together with associated arthritic changes of the joint proper.

The roentgenologic findings are considered characteristic of tuberculous disease of this joint, and are in entire harmony with the clinical study.

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EXPERIMENTAL STUDIES ON THE BIOLOGICAL EFFECTS OF RADIUM UPON TISSUES GROWING IN VITRO*

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BIOLOGICAL reactions to radiant energy have received up to the present only very scant attention, since the major interest has centered upon experimentation along physical lines. Therefore the *in vitro* cultivation of embryonal and cancer cells in artificial media outside of the body seemed especially adapted to gain a clearer insight and better understanding of the biological behavior of tissues when brought in contact with radium salts and radium emanations. In suitable media, cells will grow and multiply indefinitely; in fact some strains of cells, as fibroblasts from a chick embryo heart, have been kept alive now for over fourteen years. By this method it is possible to study growth and multiplication of different cells, and also to observe cell function and cell behavior under varied conditions. In artificial cultivation of tissues, the nutrient constituents of the media in which the cells grow are such that they furnish the necessary substances for the maintenance of cell life and cell growth. For instance, it is known that embryo tissue extracts contain nutrient substances which stimulate and promote growth activity. On the other hand, serum contains substances which inhibit and restrain multiplication and cell migration.

The knowledge of these facts afforded a starting point for further research into the reactions of growing tissues when brought in immediate contact with radiant energy. The present preliminary report deals with a group of experiments upon the inhibiting or retarding effects of radium salts and radium emanation upon embryonal and cancer cells. These studies will be continued during the ensuing year, and for the present I wish to describe only a series of experiments which deal in the main with the radiobiological effect of emanation seeds upon growing chick embryo heart and spleen and other embryonal tissues. In this connection further studies upon radiumized media to test the inhibitory and stimulating effects on embryonal tissue extracts, and also on serum, plasma, etc., are still in progress and will be reported in detail in another communication.

Chick embryo hearts from eggs incubated for seven to eleven days, and spleens removed from the chick embryos three days before hatching were used for these experiments. Small fragments of embryo heart or spleen, about 0.5 cm. in size were planted in plasma together with radium seeds containing 0.1, 0.25, 0.3, 0.4, 0.5 and 1 millicurie of emanation, for the purpose of studying the rate of growth and degree of inhibition. To control these experiments, cultures were set up, some with empty glass seeds, to eliminate the effect of the presence of a foreign body, the majority, however, without emanation seeds to afford comparative measurements.

The following is an example of a series of 100 cultures where radium emanation seeds were incorporated directly into the media Some of the seeds were placed immediately over the fragment of embryo heart or spleen, others within 1 mm. of the fragment, and still others 2 or 3 mm. distant from the tissue. Considering the separate experiments, then, as one group, 79 out of the 100 cultures lost the power to grow. In 49 there was complete absence of cell proliferation and cell migration. This was further demonstrated by the failure of these fragments to survive transference to a new medium. In 30 cultures marked inhibition was observed. There was in every case complete absence of any outwandering cells or new growth

* Read at the Tenth Annual Meeting, AMERICAN RADIUM SOCIETY, Atlantic City, N. J., May 25–26, 1925.

on the side adjacent to the radium seed, although some did show scant outwandering of cells on the distal edge of the fragment. This cannot, perhaps, be interpreted as normal growth, since these radiumized tissues did not survive subculturing over more than eight to ten days, in contrast to the control cultures which grew indefinitely, some being already in the 20th generation. The remaining 21 out of the 100 cultures seemed at first to show cell activity comparable to the controls. It soon became evident, however, that the tissues were affected by the radiation since the growth in subculture was not permanent, and the cells ultimately died within a few generations.

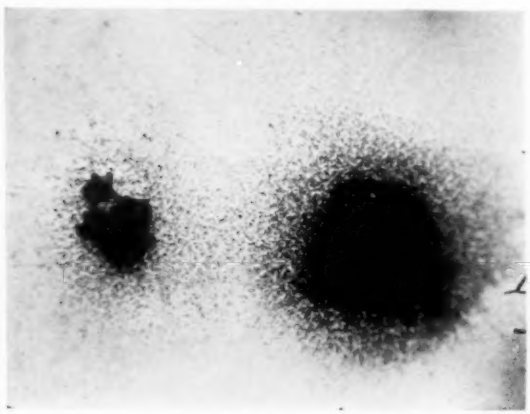


FIG. 1. Control culture, 48-hr. growth.

FIG. 2. Radium emanation seed, 0.4 mc., across tissue fragment, no outgrowth.

	Experimental					Control		
			Growth 48 Hrs.			Growth 48 Hrs.		
Exp.	No. Cult.	Mc. Radium	None	Inhib.	Fair	No. Cult.	None	Good
Total	100	0.1 to 1.0	49	30	21	138	9	129

For the control experiments tissue cultures were set up at the same time, with fragments from the same tissues, and with the same media, some cultures with empty seeds, the greater number, however, without seeds. Out of the 138 control cultures, 129 showed normal growth, and were transferred from medium to medium without difficulty.

These figures indicate that in approximately 80 per cent of the irradiated tissue cultures there was either complete loss or marked inhibition of growth, and that in 20 per cent in spite of the presence of the radiant energy, the tissues appeared to grow as in the controls. This phase of the problem will form a nucleus for further research along biophysical lines. In this connection it should be kept in mind that the results just mentioned are further complicated by the fact that we are dealing with a number of variables. In the first place the growth energy of a seven-day embryo differs from that of an eleven-day embryo. Again the serum of a young fowl is not nearly as inhibitory as that of an older fowl. Furthermore, embryo tissue extracts differ in growth-promoting activity from day to day, and, lastly, and perhaps most important, is the variation in the distance of the source of the radiation from the fragment of tissue. In accordance with the laws of the physics of radiation, each millimeter of distance reduces the absorption coefficient almost 10 times. The effect of this was clearly brought out in a set of experiments where 0.4 mc. seeds were placed immediately over the fragment. In all but one culture there was complete loss of growing power and in the one where a very scanty outgrowth was observed, this growth was at a point about 2 mm. away from the radium seed.

Exp.	Experimental: No. Cult.	Mc. Radium	Growth 48 Hrs.: None	Inhib.	Fair	Control: No. Cult.	Growth 48 Hrs.: None	Good
#98	8	0.4	7	1	0	16	0	16

In another set of experiments 17 cultures were set up with 0.1 mc. emanation seeds and in 16 there was either no growth at all, or marked inhibition.

Exp.	Experimental: No. Cult.	Mc. Radium	Growth 48 Hrs.: None	Inhib.	Fair	Control: No. Cult.	Growth 48 Hrs.: None	Good
#2264	17	0.12	10	6	1	41	2	39

Moreover it seemed that larger quantities of radium emanation up to 1 mc. did not materially increase the inhibitory results, and strange to say, in cultures where 1 mc. of radium emanation was allowed to act upon the embryonic tissue at 2 or 3 mm. distance, the inhibitory effect was not entirely complete. In other words the nearness of the source of radiation to the tissue fragment seems to be of far greater importance than the intensity of the radiant energy itself.

These preliminary studies have furnished important biological leads, and further study will indicate quantitative as well as qualitative evaluations of the principles involved in the biology of radiation. Especially is this true if a pure strain of fibroblasts with constant factors of distance, and standardization of radiant energy is made use of.

It may of course be argued that these elementary studies in the biology of radiumized tissues, growing outside of the organism, in artificial media, are not quite analogous to biological processes within the body. In the complex organism, the cellular elements of the body fluids, the cell reaction around the lesion and the character of the tissue involved, aside from any other factors, must be taken into consideration.

In addition, we must realize that we are dealing here with experimental observations of the restraining effect of radiant energy upon tissue cells possessing a very high degree of growth energy. However, the rate of proliferation of cancer tissue *in vitro* does not approach or conform by far to the heightened cell activity of chick embryo tissues. This was demonstrated in one set of experiments where 5 and 10 mg. needles of radium element were placed upon the mica cover glass directly over the cancer fragment for two to four hours, and the cultures observed after forty-eight hours in the incubator. Notwithstanding the relatively short time of irradiation, the outgrowth from the original mass was somewhat retarded, and upon microscopical examination of stained preparations, the cells presented marked vacuolization, with a high degree of degeneration. Moreover, further transfer of the cultures from medium to medium resulted in the cells finally going to pieces in eight to ten days, i.e., results similar to those obtained by Wood and Prime, with doses of 700 mg-hr.

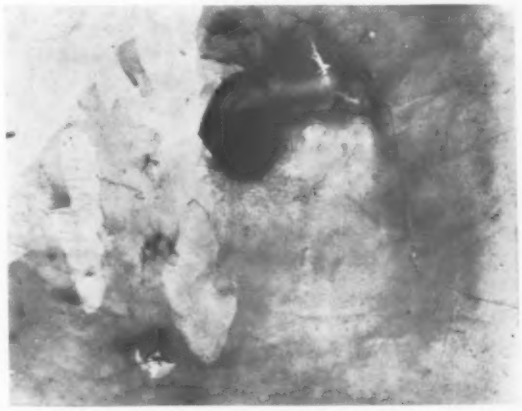


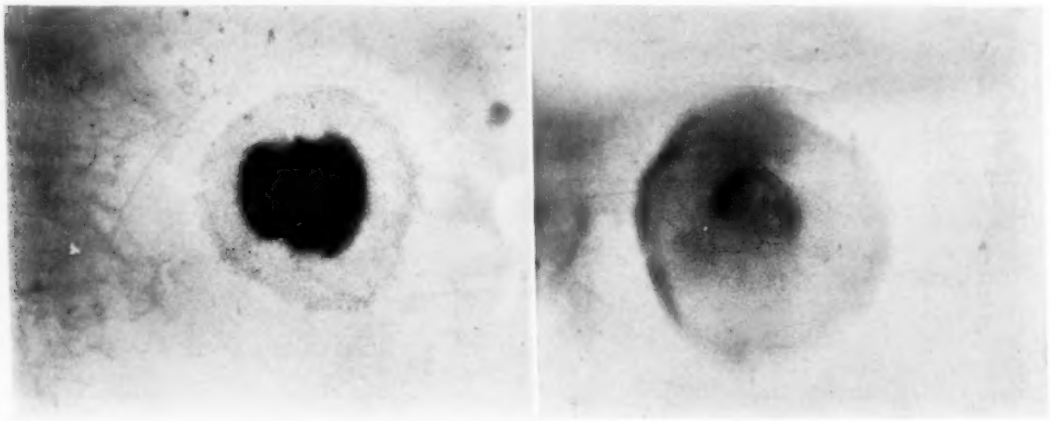
FIG. 3. Radium emanation seed, 0.4 mc., across tissue fragment; scanty outgrowth, distal side.

After all, our interest in the biological behavior of radiumized tissue is centered in the exact phenomena which have to do with inhibition or destruction of malignant cells in the organism.

In our experiments there was clearly demonstrated that there is a direct inhibitory effect upon the cellular out-growths

of the tissues themselves, regardless of the possible alteration of the media in which they were maintained. Moreover, the failure and marked retardation of cell migration and proliferation would indicate that the radiant energy *per se* exerts a direct inhibitory and restraining influence upon nuclear division, proliferation and regeneration. Histologically it can be demonstrated that the cell nuclei in the outshoots of the new tissue are markedly affected. The stained preparations of tissues growing in contact with emanation seeds show already after three days distinct pycnotic character of the nuclei. In other words, the nuclear apparatus is irreparably damaged so that the possibility of further mitosis and regeneration cannot be considered.

Aside from the evidence of direct destruction of cellular elements due to the action of the radiant energy, it is permissible also to ascribe to the radiation effects an increase in the retarding influences of the media in which the tissues grow. Experiments which are now in progress afford us sufficient lead to probe into the indirect effect of radiation through its affect upon the media. It will be possible perhaps to indicate that retardation of growth may be increased at will either by overcoming the effect of growth stimulating substances, on the one hand, or, on the other, by rendering the action of the depressing substances more pronounced. At present there are sufficient grounds to suggest that radiant energy exerts powerful influences upon both the nuclear structures of the cell itself and upon the inhibitory factors of the media. At any rate this method of biological study, duplicating as near as possible the natural life processes, promises accurate data, and will probably throw some light upon whether we are dealing with an interference with the purely reproductive or purely nutritive processes of cell life.[1]



a *b*

FIG. 4*a* and *b*. Degeneration in outgrowth. Irradiated serum used in culture medium.

ABSTRACT OF DISCUSSION

DR. RAYMOND HUSSEY, New Haven, Conn. Dr. Sittenfield has only indicated briefly some of the high points in the experimental work he has under way and it is rather difficult at this time to make any definite interpretation of the results as they have been presented. It is of interest to consider just what the therapist accepts in the way of experiments that will help him in his work. I find on talking with different men who are getting good results that none of them are doing any of their work the same way. It seems that it does not make any difference just how the work is done, just so one gets good results. Most men do not know much about the therapeutic action of digitalis or salicylate of soda, and yet they do not hesitate to use them when they think they are indicated.

As an item of general information, the idea of so-called direct and indirect effect of irradiation belongs more to poetry than it does to fact. We know of no substance that has any effect upon any cell of the body that we could not

[1] I wish to express my appreciation to Dr. Muir, who supplied the radium emanation seeds used in these experiments.

regard as an indirect one. Erythema does not appear for some time after the application of the irradiation. The same is true of sunburn, but the interval is much less. It is true, also, of the liver abscess resulting from narcosis. We can prove that it is not until the third or fourth day that function tests show the effect upon the liver cell. We have what we might call secondary effect, and yet it must take place at the time the chloroform is in the circulation.

Dr. George E. Pfahler, Philadelphia. One of the most interesting points brought out by Dr. Sittenfield was the effect of the radiation on the nutrition media preceding the implantation of the growth and the secondary degeneration. It confirms the studies made by Murphy and his co-workers at the Rockefeller Institute of the effect of radiation on tumor tissue and the subsequent degeneration that follows implantation and subsequent radiation. We have been in the past attributing most of the action to the direct destructive effect of the radiation on the tumor tissue. I have believed for a long time that we are affecting both. I believe in the destructive effect upon the tumor tissue and I also believe we have an effect on the circulating and surrounding tissues, as brought out in this work and that of Murphy.

Dr. Sittenfield (closing). I also feel that our biological studies are what will give us progress in our science. We have a right to demand and expect that progress must depend not only upon studies in physics but in biology. The life of a fragment of tissue, or the life of the one individual cell in the medium, depends upon the substance extracted and this substance is contained in the embryo tissu ande juices. Radium or the roentgen ray, or any other radiant energy, has a destructive action upon this growth-promoting substance. It destroys it or damages it or injures it considerably and causes, instead of stimulation of growth, inhibition of growth. We have, on the other hand, substances contained in serum which are inhibitory and by means of radium we can make this inhibitory power still more pronounced. Those are the effects we are aiming at in addition to destroying the cell itself.

THE AMERICAN JOURNAL OF ROENTGENOLOGY AND RADIUM THERAPY

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Publishers: PAUL B. HOEBER, INC., NEW YORK

Issued Monthly. Subscription $10.00 per year, $11.00 in Canada and $12.00 in foreign countries. Advertising rates submitted on application. Editorial office, 1909 Massachusetts Ave., N.W., Washington, D.C. Office of publication, 67-69 East 59th Street, New York

Information of interest to all readers will be found on page i. Lists of officers of The American Roentgen Ray Society and The American Radium Society will be found below

Officers and Standing Committees

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Publishers: PAUL B. HOEBER, Inc., 67-69 E. 59th St., New York City.

Twenty-seventh Annual Meeting: Book-Cadillac Hotel, Detroit, Michigan, May 18-21, 1926.

THE AMERICAN RADIUM SOCIETY

President: DOUGLAS QUICK, 350 Park Ave., New York City; *President-Elect:* ALBERT SOILAND, Los Angeles; *First Vice-President:* B. F. SCHREINER, Buffalo; *Second Vice-President:* G. W. GRIER, Pittsburgh; *Secretary:* E. C. ERNST, St. Louis; *Treasurer:* S. M. WITHERS, Denver.

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Eleventh Annual Meeting: Baker Hotel, Dallas, Texas, April 19 and 29, 1926.

Committee on Arrangements: CHARLES L. MARTIN, Dallas, Texas, JOHN W. CATHCART, El Paso, Texas, OSCAR L. NORSWORTHY, Houston, Texas.

EDITORIALS

HIGHLY PENETRATING RAYS OF COSMIC ORIGIN

ROBERT A. MILLIKAN has lately made another addition to his many contributions to our knowledge of the origin and nature of radiant energy. He gives an account of this latest contribution in an article in *Science*,[1] originally presented before the National Academy of Sciences on Nov. 9, 1925. The quotations below are from the above mentioned paper.

He has, in short, proved that extraordinarily penetrating rays exist which have their origin somewhere outside of the earth, which are constantly striking the earth from every direction, and whose shortest wave lengths are but one fiftieth of that of the hardest gamma rays of radium and but one ten millionth that of ordinary light.

The original observation on which Millikan's work is based was made by Rutherford and McLennan in 1903. They "noticed that the rate of leakage of an electric charge from an electroscope within an air-tight metal chamber could be reduced by enclosing the chamber within a completely encircling metal shield or box with walls a centimeter or more thick. This meant that the loss of charge of the enclosed electroscope was not due to imperfectly insulated supports, but must rather be due to some highly penetrating rays, like the gamma rays of radium, which could pass through metal walls as much as a centimeter thick and ionize the gas inside." It was at first assumed that the radiation thus brought to light was due to radioactive substances in the earth but it was subsequently discovered by German investigators that it did not decrease as rapidly with altitude as it should if the earth were its source. Millikan himself in 1922 verified the findings of the German investigators that the penetrating radiation was greater high above the earth than at the earth's surface, but he found that the amount of the increase was not more than one-fourth of that predicted by the German observers. Two years later the latter reduced their estimates so that they were no longer in conflict with Millikan's findings.

Further experiments by Millikan at Muir and Arrowhead Lakes "brought to light altogether unambiguously a cosmic radiation of such extraordinary penetrating power that the electroscope reading kept decreasing down to a depth of 45 feet below the surface. The atmosphere above the lake was equivalent in absorbing power to 23 feet of water, so that we had found rays, coming into the earth from outer space, so penetrating that they could pass through 45 plus 23, equalling 68 feet of water or the equivalent of 6 feet of lead, before being completely absorbed. This represents rays much harder (more penetrating) than any which had before even been imagined.

"The most penetrating X-rays which we produce in our hospitals cannot go through half an inch of lead. Here were rays originating somewhere out in space, at least a hundred times more penetrating than these."

The experiments indicate that these new high frequency rays are not homogeneous but have a measurable spectral distribution. Calculation shows that the shortest wave length is 0.0004 Å., and the longest 0.00067 Å.

The following quotation gives some idea of Dr. Millikan's conclusions with regard to the origin of these high frequency rays:

"We can draw some fairly reliable conclusions as to the origin of these very penetrating and very high frequency rays. The most penetrating rays that we have known anything about thus far, the gamma rays of radium and thorium, are produced only by nuclear transformations within atoms. This means that they are produced

[1] MILLIKAN, ROBERT ANDREWS, High-frequency rays of cosmic origin. *Science*, Nov. 20, 1925, lxii, 445–448. Copyright, 1925, by Science Service, Inc.

by the change of one atom over into another atom, or by the creation of a new type of atom. It is scarcely possible then, to avoid the conclusion that these still more penetrating rays which we have been studying are produced similarly by nuclear transformations of some sort. But these transformations must be enormously more energetic than are those taking place in any radioactive changes which we know anything about. For the frequency of any emitted ray is, according to our present knowledge, proportional to the energy of the subatomic change which gives birth to it. We can scarcely avoid the conclusion, then, that nuclear changes having an energy value perhaps fifty times as great as the energy changes involved in observed radioactive processes are taking place all through space, and that signals of these changes are being sent to us in these high frequency rays."

We have before in these pages remarked upon the ability of Dr. Millikan, rare among scientists, to render abstruse scientific data understandable and even interesting to the layman. His article in *Science*, from which the above quotations are made, is especially remarkable for its lucidity and the absence of technical terms which are often the veriest jargon to all except the specialist in the branch of science under discussion. We venture to state that the progress of civilization would be more rapid if all scientists would cultivate a style which would make their writings understandable to educated people outside of their own restricted field. The effect of the discovery of the high frequency "cosmic ray" upon the popular mind is reflected in the following quotation from an editorial in the *New York Times:*

"The mere discovery of these rays is a triumph of the human mind that should be acclaimed among the capital events of these days. The proposal that they should bear the name of their discoverer is one upon which his brother-scientists should insist. The power of these rays to pass through six feet of solid lead has suggested the name 'penetrating rays,' and the fact that they are immigrants upon this vapor sphere has suggested the name 'in-coming rays'; but they would more appropriately bear the name of the penetrating mind that passed through the miles of space to the far frontiers of our atmosphere and there met these strange forces of the universe coming out of space—the mind that lived among them for years to learn their ways, and at last brought us word of their mysterious existence. 'Millikan rays' ought to find a place in our planetary scientific directory all the more because they would be associated with a man of such fine and modest personality."

Subscribers to THE AMERICAN JOURNAL OF ROENTGENOLOGY AND RADIUM THERAPY *visiting New York City, are invited to make the office of* THE JOURNAL (*69 East 59th Street, New York*) *their headquarters. Mail, packages or bundles may be addressed in our care. Hotel reservations will gladly be made for those advising us in advance; kindly notify us in detail as to requirements and prices. List of operations in New York hospitals on file in our office daily.*

SOCIETY PROCEEDINGS, CORRESPONDENCE AND NEWS ITEMS

Items for this column solicited promptly after the events to which they refer.

MEETINGS OF ROENTGEN SOCIETIES

WE contemplate the publication of a list of roentgen society meetings such as that below, in each issue of the Journal, gradually adding other home and foreign societies as the information reaches us. Secretaries of societies not here listed are requested to send the necessary information to the editor.

AMERICAN ROENTGEN RAY SOCIETY
Secretary, Dr. Charles L. Martin, Dallas, Texas.
Meets annually.

SECTION ON RADIOLOGY, AMERICAN MEDICAL ASSOCIATION
Secretary, Dr. M. J. Hubeny, 25 E. Washington St., Chicago, Ill.
Annual meeting, Dallas, Texas, April 19–23, 1926.

THE RADIOLOGICAL SOCIETY OF NORTH AMERICA
Secretary, Robert J. May, St. Luke's Hospital, Cleveland, Ohio.
Annual meeting, Milwaukee, Wis., Nov. 29–Dec. 3, 1926.

RADIOLOGICAL SECTION, SOUTHERN MEDICAL ASSOCIATION
Secretary, Dr. Sherwood Moore, St. Louis, Mo.
Annual meeting, Atlanta, Georgia, Nov. 15–18, 1926.

THE CANADIAN RADIOLOGICAL SOCIETY
Secretary, Dr. E. C. Brooks, Montreal.
Annual Meeting Victoria, B. C., during week of June 21–25, 1926.

CENTRAL ILLINOIS RADIOLOGICAL SOCIETY
Secretary, Dr. C. J. McCullough, Decatur, Illinois.
Regular meetings held quarterly.

CHICAGO ROENTGEN SOCIETY
Secretary, Dr. Edward S. Blaine, 5 S. Wabash Ave.
Meets monthly on second Friday from October to May (except during month of December) at Virginia Hotel. Dinner at 6 P.M., scientific session at 8 P.M.

CLEVELAND RADIOLOGICAL SOCIETY
Secretary, Dr. E. P. McNamee.
Meetings are held at 6 o'clock at the University Club, on the fourth Monday evening of each month from September to April, inclusive

DETROIT ROENTGEN RAY AND RADIUM SOCIETY
Secretary, Dr. Henry L. Ulbrich, 1130 E. Grand Blvd.
Meets monthly on second Friday from October to May, at Wayne County Medical Society Building.

THE NEW ENGLAND ROENTGEN RAY SOCIETY
Secretary, Dr. Charles W. Blackett, 35 Bay State, Rd., Boston, Mass.
Meets monthly on third Friday, Boston Medical Library.

NEW YORK ROENTGEN SOCIETY
Secretary, Dr. Eugene V. Powell, 217 East 42d St.
Meets monthly on second Monday, New York Academy of Medicine.

PACIFIC COAST ROENTGEN RAY SOCIETY
Secretary, Dr. Harold B. Thompson, Seattle, Wash.
Two meetings a year.
Meets in Victoria, B. C., during week of June 21–25, 1926.

ROENTGEN RAY SOCIETY OF CENTRAL PENNSYLVANIA
Secretary, Dr. W. E. Reiley, Clearfield, Penna.
Two meetings a year, April and October.

PHILADELPHIA ROENTGEN RAY SOCIETY
Secretary, Dr. Eugene Pendergrass, University of Pennsylvania, Philadelphia.
Meets monthly on first Thursday evening, Pennsylvania Hospital.

ST. LOUIS ROENTGEN CLUB
Secretary-Treasurer, Dr. L. R. Sante, Metropolitan Building.
Meets first week of each month. Time and place of meetings designated by president.

TEXAS RADIOLOGICAL SOCIETY
Secretary, Dr. Davis Spangler, Dallas, Texas.

RADIOLOGICAL SECTION, AUSTRALASIAN MEDICAL CONGRESS
Secretary, Dr. C. A. Anderson, The Hospital, Dunedin.
Meets at Dunedin, New Zealand, during February, 1927.

BELGIAN SOCIETY OF ROENTGENOLOGY
Secretary, Dr. J. Boine, Avenue des Alliés, 134, Louvain (Belgium)
Meets monthly on second Sunday at d'Egmonds Palace, Brussels, except in the summertime.

BRITISH INSTITUTE OF RADIOLOGY
Secretary, Dr. John Muir, 32 Welbeck St., London, W. 1.
Meets at 32 Welbeck St., but regular dates and times of meeting have not yet been arranged.

THE BRITISH RÖNTGEN SOCIETY
Meets on the first Tuesday of each month from November to June inclusive, at 8.15 P.M., at the British Institute of Radiology, 32 Welbeck St., London; W. 1.

RADIOLOGICAL SECTION, NEW ZEALAND BRITISH MEDICAL ASSOCIATION
Secretary, Dr. P. C. Fenwick, The Hospital, Christchurch.
Meets annually.

ASSOCIATION OF GERMAN ROENTGENOLOGISTS AND RADIOLOGISTS IN CZECHO-SLOVAKIA
Secretary, Dr. Walter Altschul, German University, Prag, II/52.
Annual Meeting in Prag the last week of October.

DUTCH SOCIETY OF ELECTROLOGY AND ROENTGENOLOGY
Meets in Amsterdam every second month except in the summertime.

SOCIETA ITALIANA RADIOLOGIA MEDICA
Secretary, Professor M. Ponzio, University of Torino, Torino.

ELECTRO-THERAPEUTIC SECTION OF THE ROYAL SOCIETY OF MEDICINE (CONFINED TO MEDICAL MEMBERS)
Meets on the third Friday of each month during the winter at 8.30 P.M. at the Royal Society of Medcine, 1 Wimpole St., London, W. 1.

SCANDINAVIAN ROENTGEN SOCIETIES
The Scandinavian roentgen societies have formed a joint association called the Northern Association for Medical Radiology, meeting every second year in the different countries belonging to the Association. Each of the following societies meets every second month except in the summertime:

SOCIETY OF MEDICAL RADIOLOGY OF SWEDEN
Meets in Stockholm.

SOCIETY OF MEDICAL RADIOLOGY IN NORWAY
Meets in Oslo.

SOCIETY OF MEDICAL RADIOLOGY IN DENMARK
Meets in Copenhagen.

SOCIETY OF MEDICAL RADIOLOGY IN FINLAND
Meets in Helsingfors.

THE MAY MEETING

AMERICAN ROENTGEN RAY SOCIETY

The Twenty-seventh Annual Convocation of the American Roentgen Ray Society will be held at Detroit, May 17 to 21, 1926. Sessions, exhibits and headquarters will be in the Book-Cadillac hotel. Local arrangements are in charge of Dr. W. A. Evans, 10 Peterboro St., Detroit. Besides the customary features of the formal program, the banquet and the Caldwell Lecture, a day will be spent in Ann Arbor for instruction and recreation.

VISIT TO ANN ARBOR

Wednesday morning at nine o'clock the members will leave by motor bus for Ann Arbor, where an entertaining program has been arranged by Dr. Hickey. On their arrival, Prof. Randall, of the department of physics, will give, in the amphitheater of the physics building, a special demonstration on the newer experiments of the electron structure. At the new hospital, Dr. Haynes, the superintendent, will serve luncheon to the visitors. After lunch a program will be presented in the hospital amphitheater by the hospital staff and members of the *x*-ray department. For those who wish to play golf, opportunity will be afforded at the Ann Arbor Country Club. The visitors will depart at four-thirty, arriving in Detroit in time for dinner and the Caldwell Lecture.

CALDWELL LECTURE

Prof. T. Wingate Todd, F. R. C. S., head of the department of anatomy, Western Reserve University, Cleveland, Ohio, will deliver the Caldwell Lecture on Wednesday evening, May 19. His subject will be, "The Rôle of Radiology in Medical Education."

In the course of his lecture, Dr. Todd will discuss the following themes: Effect of the use of roentgen-ray methods upon anatomical instruction; anatomy of the living; the medical student as a laboratory animal; the psychology of darkness; the advantage to roentgenographic science of the examination of large numbers of known healthy young subjects: the possibility this offers for adequate record of the "normal"; application to special systems —locomotor, alimentary, genito-urinary, respiratory, vascular; adjuncts of the roentgen ray; the stereoscopic roentgenogram; possibilities of this for a students' working library; prospects for the cinematographic roentgenogram.

BANQUET

Dr. C. C. Little, president of the University of Michigan, will speak at the banquet, Thursday evening, May 20. Dr. Little is one of the youngest university presidents in America. He is well known to roentgenologists by reason of his experimental work on the biologic effects of roentgen rays. His subject will be of unusual interest.

FOREIGN GUESTS

Among the distinguished guests from abroad who will participate in the meeting are C. Thurstan Holland, president of the International Congress, and Prof. Arthur Schüller, of Vienna, whose book on cranial radiography is well known.

SCIENTIFIC EXHIBIT

The scientific exhibit will be the largest and best ever shown in America, and to

see it will be well worth a trip across the continent. Dr. Lawrence Reynolds, 10 Peterboro St., Detroit, chairman, Dr. M. C. Sosman, and Dr. B. H. Nichols comprise the committee. Among the exhibits already arranged for are foreign bodies in the bronchi, Dr. Manges; brain tumors, Dr. Sosman; cholecystography, Dr. Sherwood Moore; lesions of the genito-urinary tract, Dr. Nichols; facial tumors, Drs. Martin and Martin; pneumonoconiosis, Dr. Pancoast; gastro-intestinal lesions, Dr. Carman; bone tumors, Dr. Meyerding; some phases of crystallography, Boston Institute of Technology; and roentgenograms of mummies in the Field Museum. This is only a partial list, but gives a hint of its magnitude and educational value. It is planned to have competent demonstrators at the exhibit throughout the meeting.

To stimulate wider and continued interest prizes will be offered, consisting of a gold medal for the best exhibit, and a certificate for the next best.

Members are urged to cooperate with the committee and advise it at once of projected exhibits.

COMMERCIAL EXHIBIT

The commercial exhibit, under the direction of Dr. Christie, will be larger and better than ever before. Exhibitors desiring space should make application at once to Dr. A. C. Christie, 1909 Massachusetts Ave., Washington, D. C.

THE SCIENTIFIC PROGRAM

The program is not yet arranged as to details of time and order in which the papers will be presented, but a list of the essayists and a partial list of subjects is published below.

R. D. CARMAN
President Elect.

PRELIMINARY LIST OF PAPERS

W. F. MANGES, M.D. Philadelphia, Pa.
Foreign Bodies in the Esophagus.

G. W. GRIER, M.D. Pittsburgh, Pa.
Roentgen-Ray Treatment of Keloids.

W. F. BRAASCH, M.D. Rochester, Minn.
Ureterography.

W. A. EVANS, M.D. Detroit, Mich.
A Roentgenologic Study of Mastoid Disease.

P. M. HICKEY, M.D. Ann Arbor, Mich.
Sex Problems.

A. C. IVY, M.D.
B. H. ORNDOFF, M.D. Chicago, Ill.
Effects of the Roentgen-Ray on the Pancreas.

W. A. LAWRENCE, M.D. Memphis, Tenn.
The Therapeutic Uses of Ultraviolet Radiation.

G. E. PFAHLER, M.D.
J. B. KLAUDER, M.D. Philadelphia, Pa.
J. L. MARTIN, M.D.
Experimental Studies of the Combined Effects of the Roentgen Rays and Ultraviolet Rays.

ROSS GOLDEN, M.D. New York City
The Roentgenologic Treatment of Rheumatic Endocarditis, with Electrocardiographic Changes.

A. H. PIRIE, M.D. Montreal, Canada
Diseases of the Chest Demonstrated by Lipiodol.

H. K. PANCOAST, M.D. Philadelphia, Pa.
Roentgenologic Diagnosis of Hepatic and Subdiaphragmatic Abscesses.

ELDRIDGE L. ELIASON, M.D. Philadelphia, Pa.
Postappendicial Hepatic Abscess.

C. L. MARTIN, M.D. Dallas, Texas.
Hunger Pain.

GEO. E. PFAHLER, M.D. Philadelphia, Pa.
The Measurements of the Liver by Means of the Roentgen Rays.

W. H. STEWART, M.D. New York City.
Cholecystography by the Oral Method; An Analysis of the Last 100 Cases.

ARTHUR SCHÜLLER, M.D. Vienna.
Sella Turcica.

G. FAILLA, PH.D. New York City.
The Practical Measurement of the X-Rays.

J. W. PIERSON, M.D. Baltimore, Md.
Bone Lesions Associated with Gaucher's Disease.

L. T. LEWALD, M.D. New York City.
Report of Four Cases of Diverticulum of the Stomach, with Remarks on the Etiology and Differential Diagnosis.

Chas. A. WATERS, M.D. Baltimore, Md.
Four Years' Experience in the Treatment of Bladder Tumors by Deep Roentgen Rays

HOWARD P. DOUB, M.D. Detroit, Mich.
The Effect of Deep Therapy over the Kidneys and Adrenals.

F. S. BISSELL, M.D. Minneapolis, Minn.
An Attempt to Appraise the Roentgenographic Method in the Diagnosis of Pulmonary Tuberculosis.

R. G. ALLISON, M.D. Minneapolis, Minn.
Resolution in Pneumonic Tuberculosis.

M. C. SOSMAN, M.D. Boston, Mass.
Diabetic Tuberculosis.

A. W. CRANE, M.D. Kalamazoo, Mich.
Mucous Colitis.

R. D. CARMAN, M.D.
A. B. Moore, M.D. Rochester, Minn.
Roentgenologic Diagnosis of Chronic Ulcerative Colitis.

J. A. Bargen, M.D. Rochester, Minn.
The Treatment of Chronic Ulcerative Colitis as Based on our Present Knowledge of its Etiology.

B. H. Nichols, M.D. Cleveland, Ohio.
The Relation of Pathologic Changes in the Lumbar Spine to Lumbago.

Edw. L. Jenkinson, M.D.
Philip Lewin, M.D. Chicago, Ill.
Diseases of Bones in Infancy and Childhood.

Wm. B. Bowman, M.D. Los Angeles, Calif.
Traumatic Lesions of the Spine.

R. D. Carman, M.D.
C. G. Sutherland, M.D. Rochester, Minn.
The Duodenal Niche.

E. C. Samuel, M.D. New Orleans, La.
Focal Infection.

Masao Tsuzuki, M.D. Philadelphia, Pa.
Experimental Studies on the Biological Actions of the Modern Hardest Roentgen-Rays.

Leopold Jaches, M.D. New York City
A Study of the Differential Diagnosis between Early Osteoplastic Metastases and Paget's Disease.

W. O. Upson, M.D. Battle Creek, Mich.
The Technique of Roentgen Colon Study

Lewis Gregory Cole, M.D. New York City
Cinematographic Film of the Stomach and Duodenal Cap

George W. Holmes, M.D. Boston, Mass.
Unusual Manifestations of Malignant Lymphoma.

Others who will present papers, titles of which will be announced later, are:

J. T. Case, M.D. Battle Creek, Mich.
E. C. Ernst, M.D. St. Louis, Mo.
C. Thurstan Holland. Liverpool, England
H. M. Imboden, M.D. New York City
J. T. Murphy, M.D. Toledo, Ohio.
G. E. Richards, M.D. Toronto, Canada.
T. A. Groover, M.D.
A. C. Christie, M.D. Washington, D. C.
E. A. Merritt, M.D.

PHILADELPHIA ROENTGEN RAY SOCIETY

The Philadelphia Roentgen Ray Society held its regular meeting on December 3, 1925, at the Pennsylvania Hospital. The scientific program consisted of the following papers:

1. Diagnosis of Portal Infections.

Surgical Aspect. By Dr. E. L. Eliason.

Roentgen-Ray Aspect. By Dr. H. K. Pancoast.

An abstract of Dr. Eliason's paper is published on page 180. The paper by Dr. Pancoast will be published in full in a future issue of the Journal.

2. Roentgen-Ray Diagnosis of Pedunculated Growths and Gastric Mucosa Prolapsing through the Pylorus into the Duodenum.

Surgical Aspect. By Dr. E. L. Eliason.

Roentgen-Ray Aspect. By Dr. E. P. Pendergrass. This paper will be published complete in an early number of the Journal.

A number of interesting films and slides were discussed following the scientific program.

Eugene P. Pendergrass
Secretary.

THE PACIFIC COAST X-RAY SOCIETY

ANNUAL MEETING

The Pacific Coast X-Ray Society will hold its annual meeting in Victoria, B. C., during the week of June 21 to 25, 1926, in conjunction with the Canadian Medical Association and the Canadian Radiological Society.

Eastern men who are planning a vacation in the West during the coming summer are urged to include Victoria in their itinerary so that they may attend this meeting.

Dr. H. B. Thompson, secretary of the Pacific Coast X-Ray Society, 118 Cobb Building, Seattle, Washington, would like to have the names at an early date of any Eastern men who contemplate attending the meeting who would like to present papers.

ORAL ADMINISTRATION OF TETRAIODOPHENOLPHTHALEIN

St. Louis Mo.,
Jan. 20, 1926.

Dr. C. D. Enfield,
Louisville, Ky.
Dear Dr. Enfield:

In your letter in the December number of the American Journal of Roentgenology and Radium Therapy you speak of the failure of disintegration and solution of variously prepared capsules of sodium tetraiodophenolphthalein. This has been the experience in my private laboratory and at the Washington University laboratory.

This failure of solution of the capsules I have been able to correlate to the acidities

of the alimentary canal and have interpreted the persistence of the sodium tetraiodophenolphthalein in its original pill or capsule form as being due to an insoluble precipitate of the dye by acid, chiefly the hydrochloric acid. This precipitate forms a coating, replacing the original gelatine capsule or other coating, and holds the pill or capsule in its original mass. My article concerning this will appear in *Radiology* in February.

I have since overcome the failure of the capsules to disintegrate by adding to them one or two grains of powdered agar-agar which is intimately mixed with the crystals of the dye, and in swelling breaks up the dye mass. Since making this addition to my capsules I have at no time encountered the opacity of the capsule masses in my films.

Very truly yours,
JOSEPH W. LARIMORE.

CHARLES ALEXANDER PFENDER

Born at Round Top, Texas, January 18, 1878, the son of Amandus Pfender and Eliza Werner Pfender. Died at Boston, Massachusetts, February 17, 1926.

Dr. Pfender obtained his preliminary education in the public schools of Round Top and Gonzales, Texas, where, after completing high school he engaged in the practice of practical veterinary science by which means he was enabled to procure sufficient funds to continue his studies, the ultimate object being the practice of medicine. With this end in view he came to Washington in 1901 and accepted an appointment as assistant in the zoology laboratory of the Department of Agriculture, and during his tenure of office was associated with Dr. Charles Wardell Stiles and Dr. Brayton H. Ransom, both well-known scientists, the latter recently deceased.

Dr. Pfender entered George Washington University Medical School in 1901, graduating with the degree of M.D. in 1905, since which time he has been actively engaged in the practice of his profession. In 1911 he began devoting his entire time to roentgenology and electrotherapy. During the world war he was appointed to serve on Medical Advisory Board No. 3 as roentgen specialist.

Dr. Pfender's ability was further recognized and such recognition was evidenced by his appointment to various hospital staffs among which may be mentioned the following: Sibley Memorial Hospital and Tuberculosis Hospital, which appointments he held at the time of his death; Georgetown University Hospital and Gallinger Memorial Hospital, which appointments he relinquished some time previously because of illness. He was for many years connected with Georgetown University Medical School in various teaching capacities and had held the professorship of roentgenology since 1919.

Dr. Pfender was a prolific writer and contributed many original articles on various subjects, but chiefly on roentgenology, to many medical journals.

He was a member of the Medical Society of the District of Columbia, American Roentgen Ray Society, Radiological Society of North America, the Helminthological Society, the Society of Parasitology, and Society of Mental and Nervous Diseases of the District of Columbia. He was also a member of the University Club of Washington and the Calvary Baptist church.

Dr. Pfender's passing leaves a gap in our ranks that will be hard to fill. As one of the foremost roentgenologists of Washington, he was invaluable as a consultant, and his scientific attainments and charming personality endeared him to a host of friends. He was an ardent Christian and his fortitude and courage in facing the inevitable calmly as he did for so long a time, bespeaks a faith that few possess.

Dr. Pfender was ill for six years and knew of his approaching end, yet he carried on unflinchingly and uncomplainingly. With his indomitable will he stayed the hand of death in the most courageous battle for life that this writer has ever witnessed. He died as he lived a God-fearing gentleman and physician.

JOSEPH F. ELWARD.

MANLY J. SANDBORN

The announcement of the sudden death of Dr. Sandborn, president of the Radiological Society of North America has come as a great shock to all who knew him. He died on February 20, in his fifty-seventh year, from acute dilatation of the heart following appendectomy.

Before his election as president, Dr. Sandborn had served as secretary of the Radiological Society for five years and at the time of his death was chairman of the staff of St. Elizabeth Hospital in his home City, Appleton, Wisconsin.

A more extended account of Dr. Sandborn's life will be published in a future number.

CHARLES C. GRANDY

It is with great regret that we announce the death of Dr. Charles C. Grandy, a valued member of the American Roentgen Ray Society. Dr. Grandy died at his home in Fort Wayne, Indiana, on February 12, 1926, of chronic nephritis, following an illness of five months.

Dr. Grandy was born July 7, 1885 in Wall Lake, Iowa and lived during his young manhood in Warsaw, Indiana. He was a graduate of Indiana University and of Rush Medical College. Upon graduation in 1911 he located in Fort Wayne and became attached to the staff of the Lutheran Hospital. During recent years he has been a member of the Duemling Clinic as roentgenologist and radium therapist.

In addition to the American Roentgen Ray Society, Dr. Grandy was a member of the Allen County Medical Society, the American Medical Association, the Northern Tri-State Medical Association, the Radiological Society of North America and the American Institute of Electrical Engineers.

Dr. Grandy is survived by his widow and three children, Alice, Charlene and John, one sister, Miss Ruth Grandy of Fort Wayne and one brother, Frank Grandy of Indianapolis.

DEPARTMENT OF TECHNIQUE

Department Editor: DAVID R. BOWEN, M.D., Pennsylvania Hospital, Philadelphia, Pa

In this department will be published from time to time, as material is available, suggestions for improvement in technique.

A CONVENIENT AND ACCURATE METHOD OF MEASURING ROENTGEN-RAY DEPTH DOSAGE

BY J. L. WEATHERWAX, M.A., ROBERT A. BRADLEY, M.D.
Philadelphia General Hospital and Graduate School of Medicine, University of Pennsylvania

DAVID R. BOWEN, M.D. AND EUGENE T. LEDDY, M.D.
Pennsylvania Hospital — Mayo Clinic

IT is as essential to know accurately the amount of radiation delivered to deep-seated malignant growths, if we are to make the greatest possible progress in roentgen-ray therapy, as it is to know accurately the dosage of a powerful drug. The earliest attempts to study the measurement and distribution of roentgen rays at varying depths were made in Germany and resulted in the production, among others, of the charts of Dessauer and of Holfelder. By the use of the depth dosage measurement in connection with charts of cross-section anatomy it is possible to closely approximate the size and direction of a given field and to deliver a predetermined quantity of radiation into it. Failla[1] has described dosage charts based upon his own work and also a method of adapting standard cross-section anatomy charts to use with patients of varying size.

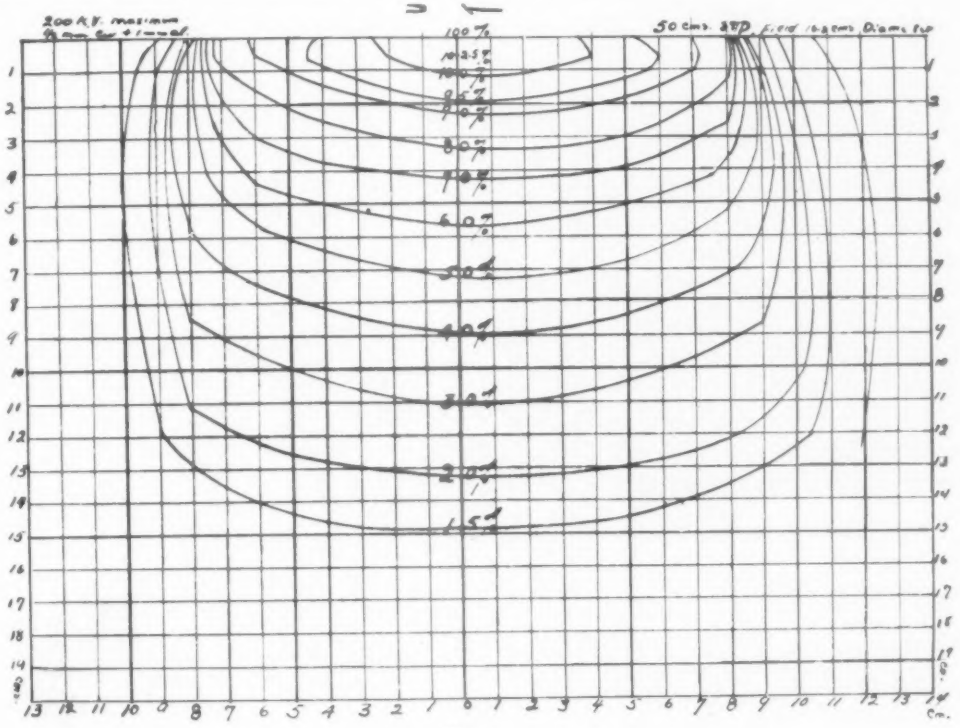

FIG. 1.

Our conversations and inquiries have, however, forced us to the belief that few roentgen therapists make actual use of any of these methods at all routinely in the treatment of patients. This paper is therefore an attempt to still further simplify these methods and to thus render their routine use more attractive.

One of us (Weatherwax) has developed a set of curves (Fig. 1) representing the distribution of roentgen rays under the following conditions: 200 kv., 50 cm. skin target distance, 0.51 mm. of copper and 1.0 mm. of aluminum as filters and a field 17 cm. in diameter. These curves represent ionization measurements of roentgen-ray intensity produced by the deep therapy roentgen-ray machine at the Philadelphia General Hospital. A modified Friedrich-Kroenig type of horn ionization chamber with an electroscopic system of our own construction was used to measure the roentgen rays. A water phantom was used to represent the patient. Ionization measurements of the roentgen-ray intensity were made on the surface of the water with the ionization chamber half submerged and this value called 100 per cent, or skin intensity. The ionization chamber was then moved about in the water in the field of radiation and ionization measurements taken at many points.

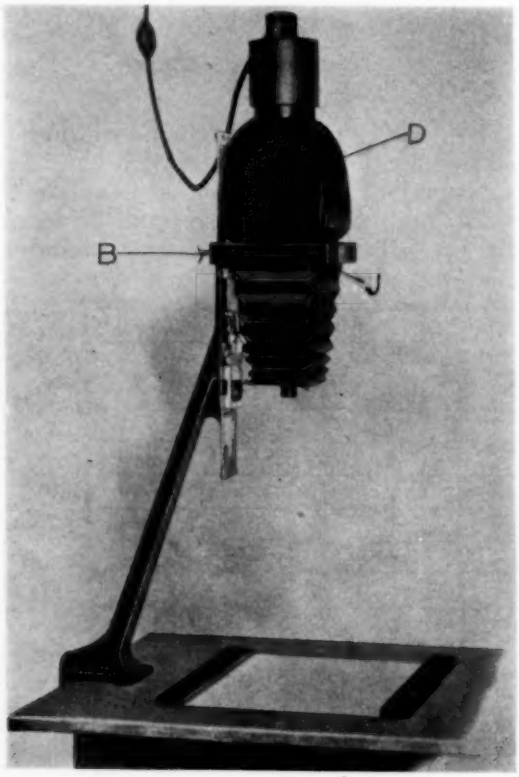

Fig. 2.

Fig. 3.

Horizontal and depth measurements of intensity at the various points were compared with measurements made in the center of the field with the ionization chamber half submerged. Intensity percentages reaching these points were computed and plotted as shown on the chart (Fig. 1). A more detailed description of our method of measuring roentgen-ray intensity can be found in previous papers.[2,3]

It will be observed that near the surface of the skin the percentage curves bend toward the primary field as they emerge. A very careful investigation of the field

just outside of the primary beam was made to determine the direction the curves would actually take. Curves illustrated by Dessauer,[4] Bachem,[5] and others show their percentage curves bending away from the primary field as they emerge at the skin. However, Failla's measurements give curves showing the distribution of radiation similar to the curves as shown in Figure 1. This is an important fact for if the percentage curves tend to converge towards the primary field, it is not necessary to make the ports of entry so far apart as if the curves continued to diverge. This point has been tested clinically and our measurements check satisfactorily.

To adapt cross-section anatomy plates to the various sizes of patients, we made use of a Kodak Auto-focus Enlarger (Fig. 2), an instrument designed for the use of amateur photographers and to be obtained in photo supply shops everywhere at a moderate price. By a coordinating action the desired enlargement of a given slide is secured by one motion, the focus being held accurate at all points automatically.

Lantern slide reproductions (size $3\frac{1}{2}'' \times 5\frac{1}{2}''$) were made from Desjardin's cross-section anatomy charts. The selected slide is placed in the enlarger slide-holder and the enlarger adjusted until the projected image, seen on a sheet of white paper on the table underneath as closely as possible approximates the predetermined size (at the same level) of the patient to be treated. A 200 watt lamp in the lamp house "D" has its light distributed through an opal glass screen to secure a uniform illumination. To read the image clearly the apparatus must be used in a darkened room or the light must be excluded by curtains arranged closely about it. A fair degree of satisfaction may thus be had with the enlarger used as delivered, but we found its use in a cabinet (Fig. 3) very much more convenient. The enlarger is mounted bottom upwards (Fig. 4). A curtain of sufficient fullness to reach around three sides is provided and the cabinet placed with the back of the curtain toward the window. The body of the observer serves to darken the fourth side. A shaft fitted with a crank serves to adjust the enlarger by means of a small wire cable fitted to it, windlass fashion. A door is provided on the side for the convenient insertion and removal of slides. The top of the cabinet is of plate glass and upon this rests a sheet of tracing paper which serves at once as the projection screen and the medium upon which the chart, now of the desired size may be permanently traced.

Curves representing a series of fields showing the roentgen-ray distribution (Fig. 1) have been reproduced in black, blue and red on thin transparent celluloid.

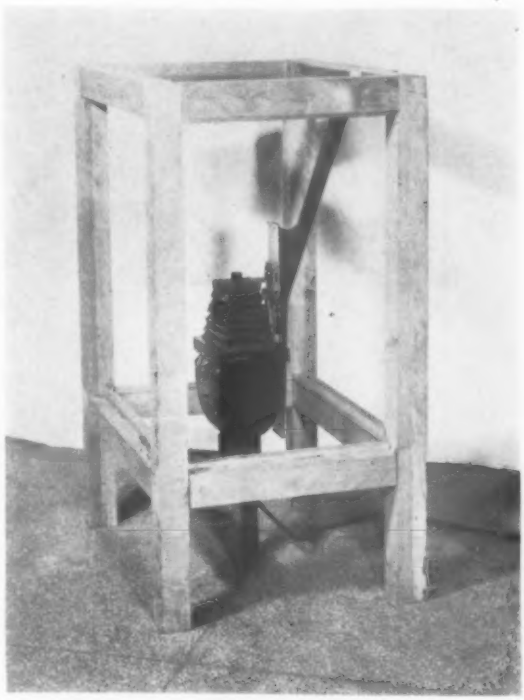

FIG. 4.

From the clinical examination of the patient, the malignant growth is located in three dimensions. At the same time the lateral and anteroposterior dimensions of the patient are obtained. Two instruments are needed for procuring the body diameter of the patient. As it will usually be desirable to make these measurements with the patient recumbent, the lateral and oblique (if needed) diameters may be made with the familiar caliper type of pelvimeter. The anteroposterior measurement can conveniently be made with a

vertical caliper of the beam compass type, the base of which rests upon the table; a movable arm is adjusted to the patient. As the patient will usually recline with some sort of mattress, or pad between the body and the table, it will be necessary to allow for the compressed thickness of this material. If there is a marked disproportion between the differential of the determined anteroposterior and lateral diameters of the patient and those of the chart, we believe it is well to consider the bent strip may now be laid about the corresponding side of the sketch and the outline corrected. The important relations are the target, the skin and the lesion. These must be determined with reference to any interfering abnormality of the patient if really creditable accuracy is undertaken.

The anatomical cross-section representing the relative position of the malignant growth is placed in the enlarger. If the apparatus, as shown in Figure 3 is used, the operator regulates the size of the image

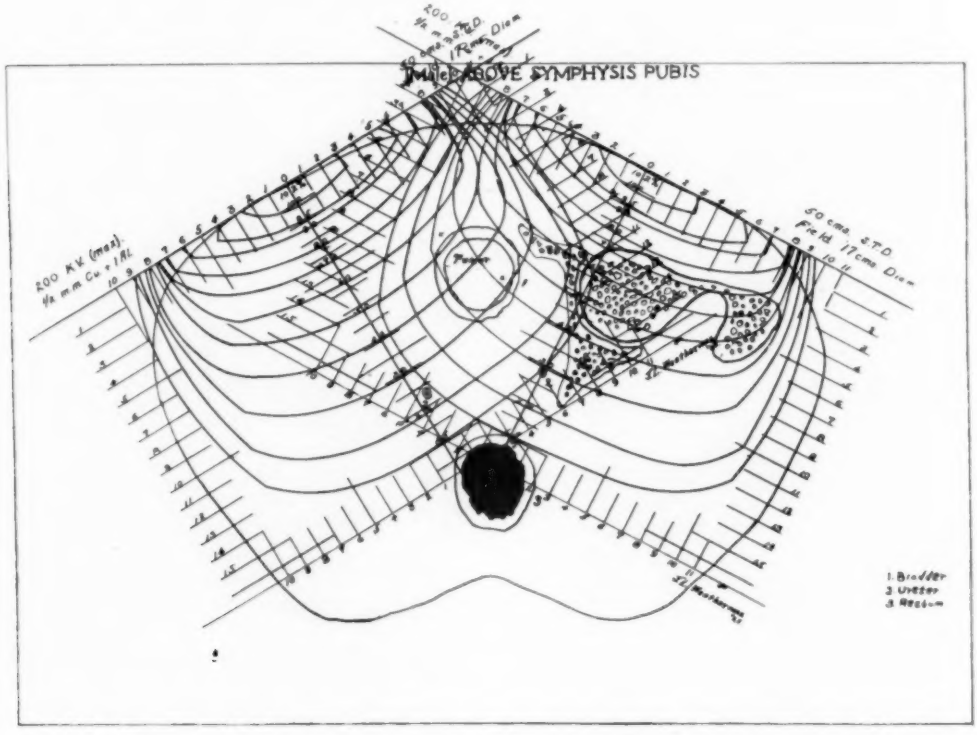

FIG. 5.

anteroposterior and make whatever allowance may be necessary for the other. This matter will be of no great importance except in the presence of deformity and obesity. When the discrepancy is so great that it must surely be a real source of error, the use of strips of rolled lead 1" × 3/32" will be found of service. With one end placed as far back between the body and the mattress as can conveniently be done, the lead strip is bent to conform to the body surface and at the anterior midline a clip marker is placed. This with his left hand by turning the handle, while with his right hand he checks the lateral and anteroposterior dimensions with the mounted movable scales on top of the apparatus. After adjustments have been made, a sketch is reproduced of the outline of the patient to be treated. At the same time the size and location of the malignant growth is also outlined by means of the three dimensions obtained at clinical examination. Other parts of the anatomical cross-section may be sketched in. This will aid in the choice of

the different ports of entry and in directing the rays so as to avoid giving too much radiation to certain organs.

The name of the patient and date are placed on the margin of the sketch. The radiologist then decides on the quantity of radiation he wishes to deliver to the malignant growth. The next step is to determine the best method of delivering this quantity of radiation and still irradiate the normal tissue as little as possible. If one port of entry delivers sufficient radiation to the malignant growth, then any one of the set of curves, say black, will give the distribution of roentgen-ray intensity. Should two ports of entry be required a second set of curves, say the red, is placed in position. The two charts will overlap and the total quantity of radiation is the sum of the percentages as read from the black and the red curves. Figure 5 illustrates the use of the red and black curves placed in position over a reproduced cross-section. Figure 6 illustrates the fields of radiation sketched on the surface, the direction of the field and percentages of skin radiation reaching different parts of the tumor and also the greatest percentage of skin radiation where the fields overlap. This same idea can be made to include a third port of entry if sufficient radiation is not delivered by the two fields. The set of blue curves is placed in position and the total quantity of radiation delivered to say any depth, is the sum of the percentages obtained from the three charts. The ports of entry, as marked on the diagram, and shown by Figure 6, act as a guide to position on the skin and direction of the rays. On the margin of the paper the voltage, milliamperage, field, filter and skin target distance are recorded. The date and number of milliampere-minutes are likewise recorded. This comprises a compact accurate record of treatment.

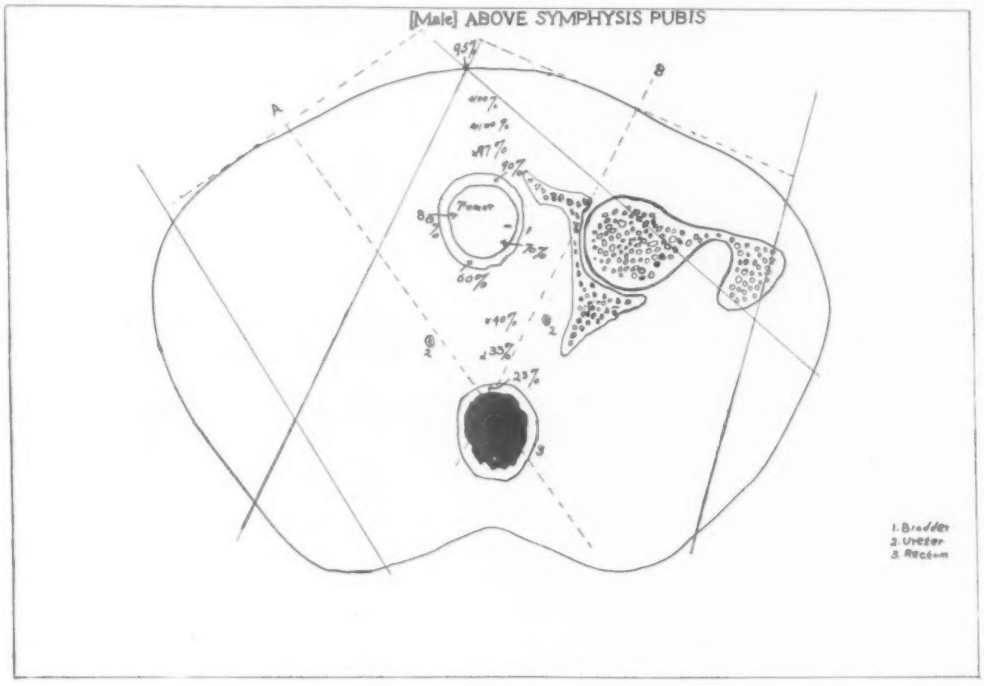

FIG. 6.

These outlines are of very great value to the radiologist in reporting a series of cases. He is able to give his exact technique as to voltage, milliampere-minutes, skin target distance, filters, field and the average percentage of the skin dosage delivered to the deep-seated malignant growths. Then the question of the size of

the patient will not enter as this factor has been eliminated by the precentage of the depth dose. It will no longer be necessary for those listening to the reports of the treatment of a series of cases to wonder how many received the same quantity of radiation into the malignant growths.

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5. Bachem. Principles of X-Ray and Radium Dosage. 1923.

AN INSTRUMENT FOR INTRODUCING NEEDLES OF RADIUM SALTS*

BY O. L. NORSWORTHY, M.D.

HOUSTON, TEXAS

THE factor of paramount importance in the use of radium rays for therapeutic purposes—that of homogeneous radiation—cannot be accomplished in all cases without imbedding radium in addition to surface application.

It is well known that deep-seated growths are less responsive to radium irradiation than superficial ones, partly because less radiation reaches the deeper growth. The overlying structures all absorb a portion of the rays passing through. In addition, the distance necessary between the container and skin reduces the efficiency of the radioactive substance. Some neoplasms, both superficial and deep, are so situated relative to important organs that surface irradiation is contraindicated. In many instances, as in the mouth, surface irradiation alone will not suffice because a lethal dose to all cancer cells would cause necrosis of large masses of normal tissue.

I believe that radium salts are as effective as radon and can be as well adapted to general use. My experience with glass seeds of radon is quite limited, though I have seen them used extensively by experienced and skilled operators in many of the large clinics. The applications were as a rule made without difficulty. However, in tumors in which two or more needles or seeds are to be implanted in the same line, I believe needles of radium salts can be placed more systematically, with more precision, with less trauma and less pain, and with greater ease than glass seeds. In making this statement I am thoroughly conscious of the large number of men of wide experience whose opinions differ with mine.

All needle inserters that I have seen are so constructed that but one needle or one seed can be implanted accurately before withdrawing the cannula entirely out of the tissues. Repeated insertion of the trocar causes pain and trauma, and it is impossible to deposit many needles or seeds in the tissues with intelligence relative to homogeneous radiation.

Trauma in or around cancer and avenues for possible infection should always be avoided when possible. By the time twenty or thirty needles of radium salt or a like number of radon seeds have been implanted by the ordinary methods now in use, the tumor has been pretty well riddled and avenues for possible infection are many. In addition, the scar tissue surrounding non-absorbable buried glass seeds furnishes a fertile field for local recurrence of the cancer.

* Read at the Tenth Annual Meeting, American Radium Society, Atlantic City, N. J., May 25–26, 1925.

There are three principal objections to the use of imbedded radium, either radon or salts: (1) the trauma produced by numerous insertions of the needle cannula; (2) inability to place the needles or seeds with exactness as related to each other, and every needle can be placed with exact knowledge as to depth and distance from its neighbor, thus making possible more homogeneous radiation. The channel in which the needles are deposited is very small, there having been but one puncture

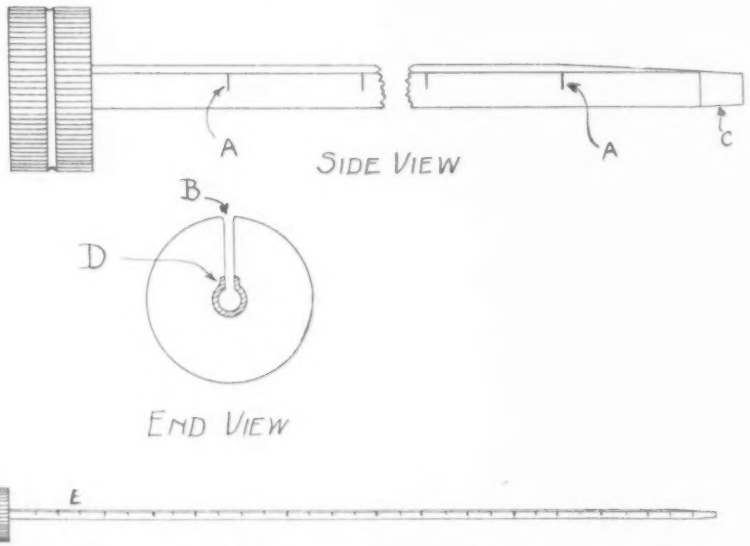

FIG. 1. Cannula. A. Graduation marks. B. Slot in side of cannula to allow passing of thread to clear instrument, to prevent jamming of plunger, or dislodgment of implanted needle. C. Cannula tapered to thin edge. D. Fin (for rigidity) on sides of slot. E. Cannula 15 cm. in length.

resulting in a lack of homogeneous radiation, and (3) holding the needles in place after implanting.

A needle inserter which I have devised for our own use has reduced these objections very materially. Trauma may be lessened in proportion to the number of needles to be inserted. If two needles or twenty needles are to be introduced in the same line the trauma will be reduced one-half or twenty times respectively. As many needles as are wanted in a straight line can be deposited at a single puncture

from the trocar, and with the point of each needle resting at the eye of its predecessor, the danger of needles slipping out is reduced to a minimum, if the patient is kept quiet in bed.

The instrument consists of a cannula, a trocar and a piston. The cannula has a caliber for carrying needles of the diameter to be used, and is graduated on the outside according to the lengths of needles to be used. The cannula has two fins with slot between extending its entire length. The fins serve to force the tissues away from the

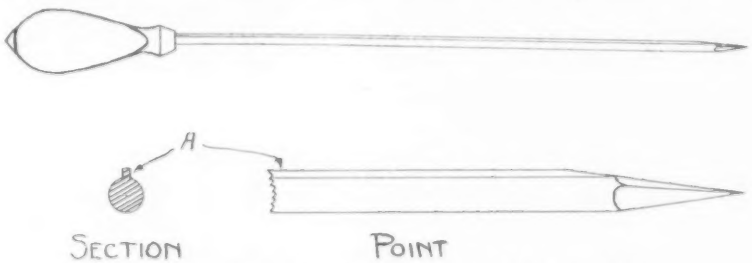

FIG. 2. Trocar. A. Fin which fits and fills slot in cannula.

cannula and form the slot through which the thread slips and also to furnish strength for the cannula. The edges of the slot through which the thread slips between the fins are especially rounded and smooth on withdrawal. We have one instrument 150 mm. and one 250 mm. long for both 5 mg. and 10 mg. needles. We have found that the 5 mg. needles will feed well through the 10 mg. cannula and we do not

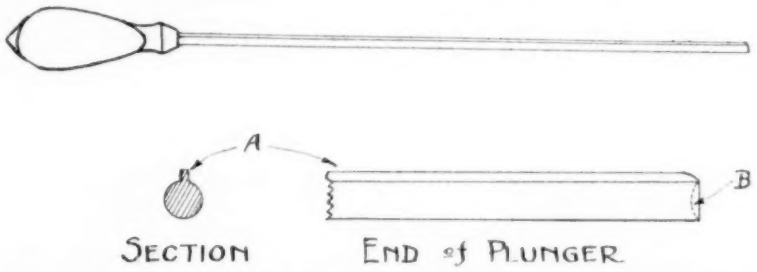

FIG. 3. Plunger. A. Fin which fits and fills slot in cannula; rounded end so that when implanting needle, thread is cleared from instrument through slot. B. End concaved to give good bearing against eye of needle.

to prevent injury to the thread. The trocar extends beyond the distal end of the cannula and has a fin fitting into the slot in the cannula which prevents the tissues from entering the slot during introduction. believe an additional cannula for the 5 mg. needles is necessary.

With a single puncture of the trocar as many needles as are required may be inserted in a straight line before with-

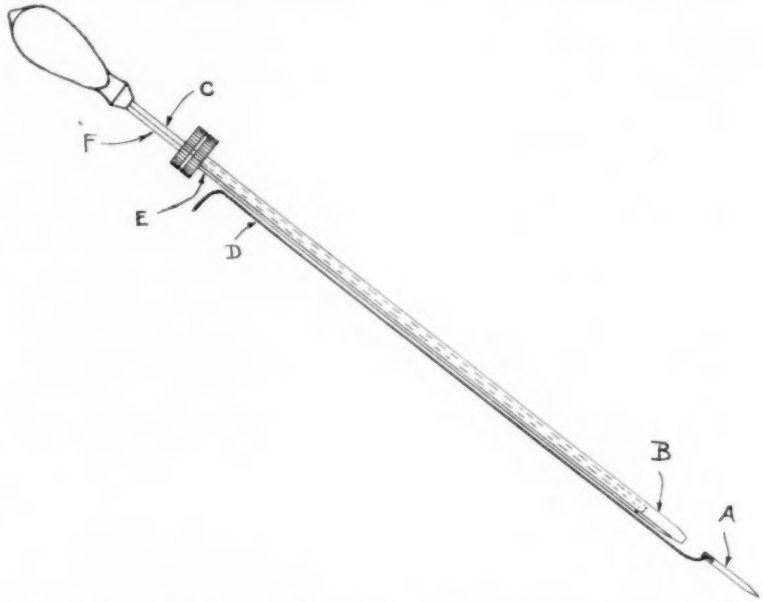

FIG. 4. Cannula with plunger (slightly withdrawn) after implanting radium needle and stripping thread from cannula. A. Implanted radium needle. B. Cannula. C. Plunger. D. Thread. E. Slot in cannula. F. Fin on plunger which strips thread from cannula.

The piston fits the cannula in the same manner as the trocar and is somewhat longer. This extra length is to insure the needle being deposited well away from the cannula and to force the thread out so that it may not bind against the cannula drawing the cannula. The trocar can be inserted again and another line of needles be deposited either parallel or perpendicular to the first. This process may be repeated until as many needles have been placed as are needed.

To insert the instrument, make a stab wound of the skin or mucous membrane sufficiently large to permit free entrance of the cannula. If this is not done it will be found that the needles cannot be deposited correctly as the cannula will slip out in jerks and will have to be forced back into the opening, thus increasing trauma. Next, push the trocar to the farthest point at once. Withdraw the trocar from the cannula and place the needle in the caliber of the cannula so that the thread will slip easily into the slot without binding between the eye of the needle and the sides of the cannula; with the piston, which has a concave end, gently push the needle forward to near the end of cannula. Now withdraw the cannula to the next mark and here implant the first needle. Remove the piston from the cannula before moving the cannula. Draw the cannula out to the point for depositing the next needle. Repeat the process until the tumor has been supplied with all needles to be implanted in that line before entirely removing the cannula from the tissues. Needles may be deposited in different directions as desired. The small non-bearing radium space between the point and eye of the needle will receive cross fire irradiation from each needle. In case of a tumor too large to be treated at one sitting, it may be diagrammed and the treatment continued later.

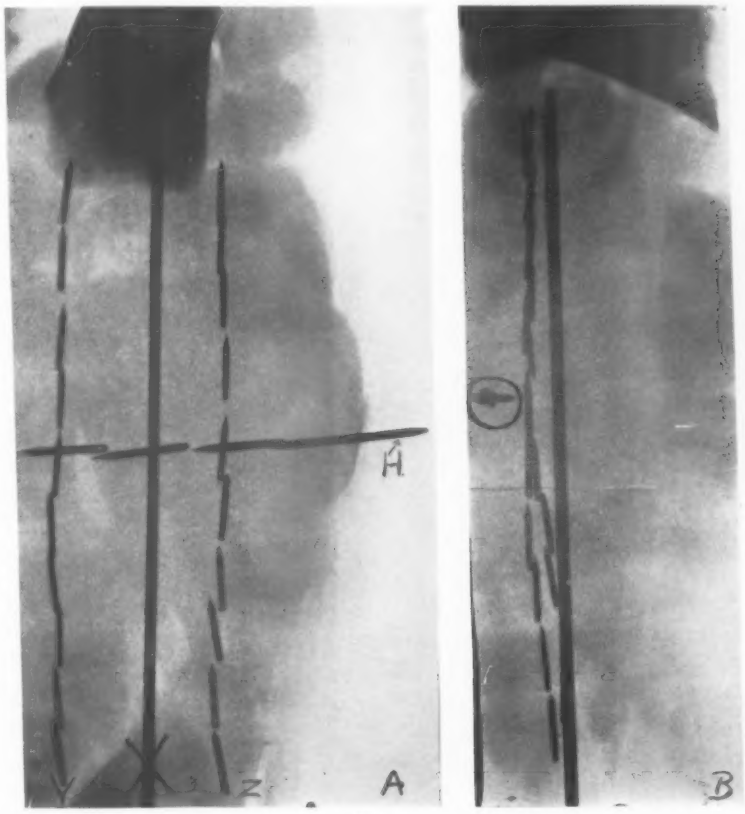

Fig. 5.

We diagram the needle lines on the surface of the tumor with picric acid as a stain. This makes accurate implantation easier. The cannula, which is graduated with 0.5 cm. divisions, is an excellent rule for this purpose.

In soft tumors better placement of needles is accomplished by inserting two trocars with cannulas at right angles to each other and in the contemplated

needle lines near the center of the tumor. These are left in place and tend to fix the tissues, prevent possible sliding of tissue and displacement of needles while depositing the first rows. Needles are then implanted through these two cannulas before their removal.

Needles may be implanted under roentgenoscopic observation, although we have not found this necessary. Figure 5 shows roentgenographically twenty 5 mg. needles and a cannula imbedded vertically and five 10 mg. needles imbedded horizontally in a beefsteak about 6 × 12 × 30 cm. in size. All of these needles and the trocar were introduced without the aid of a roentgenoscope. The needles represented by the letter "Y" were implanted carelessly, recording at the time which needles were probably out of alinement. The needles implanted unevenly correspond with our record made as they were inserted. The needles represented by the letter "Z" were implanted with more care. Figure 5B is the same as Figure 5A, with lateral exposure. Note that both vertical lines of needles and the cannula are very nearly superimposed. The irregular dot within the circle represents the horizontal line of needles endwise.

We use standard needles of radium barium sulphate, as prepared by the Radium Chemical Company of Pittsburgh, with the belief that 5 mg. non-corrosive alloy needles imbedded for twenty-four hours will give approximately the same amount of radiation as 1 mc. glass seeds of radon left permanently. Estimating that 5 mg. of radium element contained in a non-corrosive alloy needle in the form of radium barium sulphate will produce a caustic effect for 4 millimeters and autolytic degeneration for an additional 10 millimeters surrounding the full length of the needle, we place the needles from 1 to 3 cm. apart. In tumors believed to be of embryonal cell origin, where recovery is preferred by autolytic degeneration, needles are deposited from 2 to 3 cm. apart and are left imbedded for from four to twenty-four hours. In tumors of squamous cell origin, where caustic destruction is preferred, we adhere to the rule of 1 cm. between needles and leave needles imbedded for twenty-four hours.

A similar, but smaller, instrument could be constructed for platinum needles. As yet sufficient necrosis has followed in no case to warrant elimination of all the beta rays, and, as all our needles were of non-corrosive alloy, we have made no change.

ABSTRACT OF DISCUSSION

Dr. R. E. Loucks, Detroit, Mich. I would like to know what kind of thread the Doctor uses.

Dr. H. K. Pancoast, Philadelphia. I would like to know how he gets the needles out.

Dr. A. Howard Pirie, Montreal. Do I understand that you leave a bunch of thread in the wound? I should think this would favor infection.

Dr. George E. Pfahler, Philadelphia. How do you sterilize the fishing cord?

Dr. Norsworthy, (closing). If you wish to eliminate all of the beta rays, the cannula could be left in place. We have had no trouble whatever in removing the needles. We keep the threads separated so far as is possible but sometimes if you pull three or more threads, the needles will come out just the same. I use a No. 0 fishing cord which is supposed to be waterproof and to have a twelve pound tensile strength. We find that this passes through the cannula without any difficulty, is not as stiff as a waxed thread and we have had no trouble with it so far. We have placed as many as ten needles in line.

Dr. Pirie asked why the threads do not form an avenue of infection, but how can ten threads through a small hole have as much chance for infection as ten threads through ten holes? The traumatism is reduced ten times and the cicatrix ten times by planting the needles all in one line. We boil the fishing cord and then soak it in alcohol. Before using it, we dip it from this into boric acid solution.

BOOK REVIEWS

Books Received Are Acknowledged under Heading: Books Received. This must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

ALLERGY: ASTHMA, HAY FEVER, URTICARIA AND ALLIED MANIFESTATIONS OF REACTION. By William W. Duke, PH.B., M.D., Kansas City, Missouri. Cloth. Pp. 339, with 75 illustrations. St. Louis: The C. V. Mosby Company, 1925.

As far back as 1873, C. H. Blackley demonstrated conclusively that typical hayfever in its several forms is due to reaction to pollen of various sources. This observation remained largely neglected until confirmed by Dunbar in 1902 and later by Koessler, Walker, Cooke, Coca, and others. The more general problem of hypersensitiveness, specific and nonspecific, is not a mere curiosity encountered only occasionally, for we learn that about 15 per cent of individuals appear to be affected in slight or marked degree by this condition. Not only is it a common cause of illness, but frequently it is responsible for severe illness and in some instances for sudden death. It is common knowledge that specific foods and pollens are capable of producing pronounced reactions in susceptibles, but how many of us realize that purely physical factors such as light and heat and cold apparently are able to produce somewhat analogous reactions? The roentgenologist can probably recall from the literature in his field, if not from his own experience, cases of apparent hypersensitiveness to the action of radiations.

In the book before us Dr. Duke has undertaken a presentation of the subject of allergy, asthma, hayfever, urticaria and allied manifestations of hypersensitiveness primarily from the standpoint of the clinician, and numerous cases are cited in illustration of particular reactions. The larger portion of this manual is given over to a discussion of experimental anaphylaxis and serum sickness, to bacterial allergy and to illnesses in humans traceable to specific hypersensitiveness to different material agents. The general characteristics and symptoms of allergic reactions are discussed and the methods of specific diagnosis described. A chapter is given over to specific, nonspecific and symptomatic treatment.

A very important and valuable step has been taken by Dr. Duke in the introduction of a section devoted to reactions caused specifically by physical agents such as light, heat, cold, mechanical irritation, freezing and burns, and in the case of heat sensitiveness, reactions produced indirectly by the effect of mental or physical effort. Those interested in the application of physical measures to therapy or diagnosis will welcome this discussion. We find no mention of roentgen rays or radium in this section. Perhaps the author's experience has not extended to such cases or it may be that well authenticated examples are still lacking.

The presentation is concise, and theory and fact are well balanced. A little more emphasis is placed on the pollenating plants of the Middle West but this is natural, and the fact weighs very little against the general utility of this book.

B. COHEN.

BOOKS RECEIVED

THE PATHOLOGY OF TUMORS. By E. H. Kettle, M.D., B.S. Lond. Professor of Pathology and Bacteriology, Welsh National School of Medicine, Cardiff; formerly Pathologist and Lecturer on General and Special Pathology, S. Mary's Hospital and Medical School; Pathologist to the Cancer Hospital, Brompton, Second edition. Cloth. Price $5.00. Pp. 285, with 159 illustrations. New York: Paul B. Hoeber, Inc., 1925.

ULTRA-VIOLET RAYS IN THE TREATMENT AND CURE OF DISEASE. By Percy Hall, M.R.C.S. (Eng.), L.R.C.P. (Lond.). Cloth. Price, $3.75. Pp. 110, with 23 illustrations. St. Louis: C. V. Mosby Company, 1924.

THE RADIOLOGICAL EXAMINATION OF THE MALE URETHRA. By G. L. S. Kohnstam, M.R.C.S. (Eng.), L.R.C.P. (Lond.), Late House Surgeon to the Urological Department, King's College Hospital, London; and E.H.P. Cave, M.D., B.S. (Lond.), M.R.C.S. (Eng.), L.R.C.P. (Lond.), D.R.M.E. (Camb.), Late Resident Radiologist, King's College Hospital, London. Cloth. Price. $5.50. Pp. 115, with 64 illustrations. New York: William Wood and Company, 1925.

AMERICAN ANNUAL OF PHOTOGRAPHY, 1926. Edited by Percy Y. Howe. Paper. Price, $1.75. Cloth. Price, $2.50. New York: The American Annual of Photography, Inc., 1925. Sales Agents, George Murphy, Inc., 57 East 9th St., New York City.

INTERNATIONAL ABSTRACTS OF ROENTGEN AND RADIUM LITERATURE

ROENTGEN DIAGNOSIS

ELIASON, E. L., M D. Pylephlebitis and Liver Abcess Following Appendicitis.

Pylephlebitis and liver abscess are erroneously regarded by many writers as synonymous. They frequently exist in conjunction but in the series reported in this paper at least 2 cases of pylephlebitis existed without liver abscess. By far the most important single cause of this condition is suppurative appendicitis (42 per cent) (Langdon Brown). In this series all 14 cases were due to appendicitis.

Associated with the liver abscess there frequently exists a subdiaphragmatic abscess. In the cases here reported a liver abscess preceded the subdiaphragmatic in every instance.

The literature discloses in all but 53 cases of liver abscess secondary to appendicitis, with a mortality of 59 per cent. Examination of the University of Pennsylvania Hospital records of the last 2237 cases of acute appendicitis preceding the year 1922 reveals only 3 cases of hepatic abscess (0.13 per cent incidence), a figure closely resembling those quoted in the literature.

The writer has collected from the University, Howard and Philadelphia General Hospitals 14 cases in all, 10 of which were personal cases; 7 of these 10 were admitted having had their condition over weeks or months, 3 only developed liver abscess following operation for appendicitis by the writer. All of the personal cases (10) were seen since June, 1922. The fact that there is a greater incidence since 1922 leads the writer to suspect that the improved methods of diagnosis are responsible. Chief among these improvements is that of the roentgen-ray and roentgenoscope. Passing directly to these findings as being of paramount interest to the members of the Roentgen Ray Society, the other symptoms of a clinical nature will be omitted.

Roentgenograms and roentgenoscopic examinations were made in 10 cases. Negative reports were returned in only two. The other 8 cases all were reported by Dr. H. K. Pancoast as showing elevation of the right side of the diaphragm and in some instances restriction of movement on that same side. In 3 of the series there was also a shadow in the lower right chest interpreted as fluid. This shadow appeared only in those cases in which the abscess or abscesses affected the upper surface of the liver. These roentgen findings are extremely interesting as they seem to point to the fact that pus in the liver will give much the same phenomena as will subdiaphragmatic pus. In 3 of these cases there was an abscess between the diaphragm and the liver but it was the result of a rupture of a liver abscess into this space, as shown at operation, the condition being then one of the hour-glass type of abscess.

It may be stated here that in practically all of these cases the clinical diagnosis at first was a basal pneumonia or a subdiaphragmatic abscess. At operation however, in each instance, the proper diagnosis of liver abscess was made.

Mortality: Seven of the 14 lived (50 per cent). This is not as high a recovery rate as that quoted earlier in this article from the cases collected by Slesinger, namely 20 recoveries in 23 cases. It more nearly, however, approximates the mortality figure (59 per cent) of the entire number of cases, 53, collected by the writer from the literature at the time of writing. Adding the present series of 14 cases with 7 deaths, gives an average mortality of 54.5 per cent. This makes one pause, as many textbooks state that pylephlebitis is practically invariably fatal.

If a careful survey of the reported series be made, two very startling facts are brought to light. The first of these is that in every case a provisional diagnosis and often a retained diagnosis of a right basal pneumonia was made. This was based on the physical findings of a compressed lower lobe together, in some instances, with effusion. The roentgen ray eliminated the pneumonia diagnosis in each case. Therefore in looking over the cases as collected and noting the increasing frequency of diagnosis, 14 cases in 3 years in the writer's service, as compared to a previous total of 53 in the literature, one cannot help but believe that many of these cases were diagnosed and died as supposed septic pneumonias. The roentgen ray has dispelled this error in diagnosis and shown the condition as it really exists.

The second startling fact brought out is the tardiness with which a positive operative diagnosis was made. In the 3 cases that developed after an appendectomy by the writer, the diagnosis of pylephlebitis and liver abscess was made in fourteen, nineteen, and twenty days. In the cases coming to the hospital with the condition already existing, the historian proved the disease to have been

present for periods varying from two weeks to eleven months, 3 cases being respectively of eight, ten and eleven months' duration, a sad commentary on our diagnostic ability.

SUMMARY

1. Pylephlebitis and liver abscess are not identical and occur as a complication in appendicitis in from 0.1 per cent to 0.4 per cent.
2. The roentgen ray and roentgenoscope aid in early diagnosis by showing a high diaphragm sometimes with restricted movement.
3. Local edema and prominent veins are valuable signs.
4. Pain is an unreliable symptom. It is noted most when the infection is in or on the upper surface of the liver.
5. Pneumonia signs are frequently found as a result of lung compression rather than due to a pneumonia.
6. Jaundice is practically a constant symptom.
7. Lassitude and anorexia are very suggestive in this association.
8. Prognosis is not a universally bad one—54 per cent recovery.
9. Surgery is the treatment of choice.

EISENDRATH, DANIEL N. Ureteral strictures, kinks, and abnormal inserts. *Surg., Gynec. & Obst.*, November, 1925, xli, 557–564.

We are indebted to Hunner for directing attention to the necessity of using special bougies supplemented by ureteral pyelography in searching for ureteral stricture. The latter method has revealed that kinks and abnormal insertions into the renal pelvis can be more easily demonstrated than has ever before been possible. These two conditions must, therefore, also be taken into consideration when interpreting the source of symptoms such as abdominal pain, or those more strictly referable to the urinary tract.

In the roentgenogram there may be considerable deviation from the classical type of ureter. The levels at which the narrowings occur may be high or low and the narrowing may extend over an unusually large section of the ureter. In certain normal individuals a kink may be found as the result of a redundancy or the folding up of the normal ureter. Moreover, a kink may be artificially produced if only one pyelogram is taken, i.e., without withdrawing the opaque catheter and making a second exposure. Experiment indicates that the amount of fluid and pressure probably play but little part in widening the shadow of the ureter. It must be remembered, however, that inflammatory changes in the ureteral wall as a rule produce a wider shadow. The possibility of the existence of such a dilatation must be considered in the interpretation of the relatively wide shadow when stricture is suspected. It is believed that quite a number of strictures encountered in adult life may be of congenital origin. One should not draw the deduction that when a kink is seen in the ureteropyelogram it is necessarily responsible for the symptoms in a patient. Kinks are often found upon inspection of a normal ureter. If, however, there are clinical evidences of renal infection and these are confirmed by the urological study it is justifiable to state that the kink is responsible for obstructing the escape of the pelvic contents. A thorough study of the ureteropyelogram may bring to light abnormal insertions of the ureter in the pelvis which is of great value from the diagnostic standpoint and from the standpoint of treatment.

ELIASON, E. L., and WRIGHT, V. W. MURRAY. Benign tumors of the stomach. *Surg., Gynec. & Obst.*, October, 1925, xli, 461–472.

Under benign tumors of the stomach are included adenomas, papillomas, myomas, fibromas, cysts, angiomas, lipomas, osteomas, myxomas and the misnomer "polyps." Under this head diverticula, lymph node enlargements, hypertrophies, abscesses, aneurysms and indurated swellings are not included. A review is given of reported and collected cases, together with a personal collection of 50 cases. The condition is not so infrequent as is usually believed. More extended use of the roentgen ray in gastric cases with operation (early) upon gastric cases that are benign or doubtful may result in saving lives that would otherwise be lost.

By far the best diagnostic means at hand today in the diagnosis of benign tumors of the stomach is study of that organ by the roentgen ray. Once seen it presents a picture which impresses one greatly as being so different from the picture of any other condition that it may cause surprise and doubt when first observed. The single tumors which are large enough to be discerned stand out as globular, smooth, regular, clear and persistent shadows of the lesser or greater curvature, and by this very smooth, uniform outline immediately strike one as not characteristic of the irregularity of malignancy and the punched out areas of ulceration. Pedunculated tumors attached to the anterior or posterior walls may be overlooked at one roentgen examination, to be found at a subsequent one when the patient is roentgenographed in the prone position or is manipulated under the roentgenoscope. The

prone position best brings the tumor out in cases in which the tumor is not otherwise in apposition to the walls.

Hemangiomas and cysts give a clear picture unlike the appearance of any other tumor and are quite typical. Gastric polyposis presents a distinct mottled appearance not dissimilar to a bunch of grapes and is most frequently seen in the pyloric end. Diagnosis by the position the tumor occupies in the stomach cannot as yet be made with certainty as to type.

ELSBERG, CHARLES A., and SILBERT, SAMUEL. Changes in size and relations of lateral ventricles in tumors of brain. *Arch. Neurol. & Psychiat.*, October, 1925, xiv, 489–501.

A preliminary report is given of the study of the finer changes in the ventricles in tumors of the brain. This was done with the aid of actual casts of the ventricles of patients who had died from brain tumors; comparison of these casts or models with the hardened brains and the ventriculograms taken before death; and an attempted correlation of the changes found with the symptoms and physical signs which had been observed in the patients. The study comprises 31 brains, and further investigation in a larger number of cases will be necessary to completely verify the present findings.

Observations were made of the changes in the lateral ventricles in tumors in the posterior cranial fossa. An interesting finding was the change produced in the dilated lateral ventricles by subtentorial growths. The ventricle contralateral to the growth is regularly more dilated than that on the same side, contrary to the usual opinion. There was also found a remarkable change in the posterior horns which has not been described. On the same side with the tumor, the posterior horn of the lateral ventricle was consistently shorter and was displaced forward and outward as compared with the other posterior horn. Infiltrating tumors of the cerebral hemispheres usually produce a homolateral hyperplasia of greater or less degree. The effect is either to collapse or to separate more than normal the planes of the anterior and inferior horns, while on the opposite side the vertical planes through the anterior and inferior horns are more closely approximated to each other. This change should be clearly visible on anteroposterior roentgenograms of the ventricles if sufficient air has been injected to fill both the anterior and inferior horns. The present conception is that hyperplasia of a hemisphere is rarely present in dural tumors and is seldom absent in infiltrating growths. The demonstration of the presence of a hyperplasia of the cerebral hemisphere would therefore be a step in the direction of distinguishing removable from the generally non-removable supratentorial growths.

Study of the models and the ventriculograms has shown that in a hydrocephalus associated with posterior fossa new growths and with obstruction in the Sylvian aqueduct or in the foramina of Magendie and Luschka, the dilatation of the temporal horns is often relatively small as compared with the anterior horns and bodies of the lateral ventricles. In supratentorial lesions on the other hand, the dilatation of the inferior horns is as great and sometimes greater than that of the frontal horns and the bodies of the ventricles. It is not yet known how many exceptions there are to this rule.

Careful measurements were made of the sizes of the models in comparison with the sizes of the ventricles on the roentgen-ray films. The size of the shadows of the ventricles seen on the ventriculogram is somewhat exaggerated and is larger the farther away the ventricle is from the film. The difference in size of the actual model as compared with the shadow of the air-filled ventricle on the roentgenogram is less than one would expect; and even in large ventricles the difference measured in the longest diameter of the ventricle is not greater than 1 to 2 cm. It is therefore a safe assumption that the shadow of the lateral ventricle farthest away from the roentgenogram is about 1.5 cm. larger and that of the ventricle nearest the film about 1 cm. larger than the true size.

ESAU. Fractures of the os hamatum. *Fortschr. a. d. Geb. d. Röntgenstrahlen*, March, 1925, xxxiii, 201–202.

The number of fractures of the carpals is relatively great. It may be due to the fact that easily diagnosed fractures of the hand remain under the treatment of the general practitioner, while the long drawn out difficulties with carpal fractures, which are often out of proportion to the mildness of the accident causing them, force the patient to consult the roentgenologist. Fractures of the os naviculare are very frequently found in connection with other fractures. An examination of plates taken during the past five years disclosed an unexpected number of fractures of the os naviculare. Two isolated fractures of the hamatum were noted and are reported. In one case the roentgen picture showed a distinct break at the ulnar free edge with displacement of the fragment dorsally. In the second case the roentgenogram showed a longitudinal fracture of the hamatum with a narrow but distinct zone of rarefaction and displacement of the ulnar portion of the fracture toward the triquetrum.

ESAU. The importance of roentgen diagnosis in pancreatic cyst. *Fortschr. a. d. Geb. d. Röntgenstrahlen*, April, 1925, xxxiii, 358–363.

A case is described in a woman aged fifty-seven, complaining of indefinite stomach trouble. The previous history yielded nothing significant except that the patient could not eat as much food at a meal as she liked. There was, however, no loss in weight. The roentgenogram gave a striking finding. The stomach from the cardia to the pylorus was smooth and uniformly filled and drawn in a semicircle over a structure which included practically the whole subphrenic area. The tubular stomach was pushed strongly to the left, and lifted toward the diaphragm. The duodenum was likewise drawn over the spinal column toward the left. Peristalsis showed only very flat waves, but emptying of the stomach was prompt. The shadow produced by the round tumor was distinctly denser than its surroundings.

On the basis of the surprising but unequivocal roentgen finding the diagnosis was made of a probable cystic tumor of retroperitoneal origin. It was undecided whether this was a pancreatic or adrenal cyst. Echinococcus cyst was definitely excluded, because echinococcosis had never occurred in the vicinity where the patient resided. Operation disclosed cyst of the size of a child's head, containing 1.5 liters of a clear amber fluid. This cyst was located in the subphrenium away from the pancreas and in close relation to the stomach. The finding, however, of typical pancreatic lobules in the wall of this cyst established this as a pancreatic cyst. It is believed that this cyst in the early stages of development became separated from the pancreas and continued its development.

GRIER, G. W. Roentgen diagnosis of disease in the nasal accessory sinuses. *Boston M. & S. J.*, July 9, 1925, cxciii, 50–66.

If sinus roentgenology is ever to become the valuable adjunct in diagnosis that it should be the roentgenologist must have a better knowledge of sinus pathology and must understand more definitely from the rhinologist just what he expects to find out from the roentgen-ray examination. The rhinologist on his part can greatly aid the roentgenologist by giving him more operative findings so that he may gradually accumulate positive knowledge that certain definite roentgen-ray findings accompany specific pathology as demonstrated on the operating table.

A detailed description is given of the pathologic changes and the accompanying roentgen shadows produced in acute sinusitis, catarrhal and suppurative; chronic sinusitis, hyperplastic type, suppurative type, and mixed type.

If a large amount of mucous lining of a sinus is removed there will be replacement by connective tissue, and a certain amount of ossification may take place. In any event the density of the sinus is increased prominently. Therefore if one is not to be misled, the fact of previous operation must be known before interpreting the roentgen-ray findings. The roentgenogram gives information on one point only, namely, the density of substances, and it is unfair to place the burden of surgical judgment upon this diagnostic agent alone.

HAAS, LUDWIG. Experience in roentgenology of the sella. *Fortschr. a. d. Geb. d. Röntgenstrahlen*, 1925, xxxiii, 419–422; 469–494.

One of the major difficulties in the roentgenological diagnosis of the sella turcica is the difficulty in distinguishing the pathological from the normal, even in the hands of practised roentgenologists. Consequently many clinicians have come to regard a roentgen examination of the sella in diagnosis of conditions of the hypophysis as entirely unreliable. This is all due to the fact that there is as yet lacking an objective set of data on the appearance of the sella in health and in disease.

The present study is based upon 225 roentgenograms of the sella, 39 of which represented some pathology of the hypophysis, and 186 were normal sellas in sick and healthy individuals. The object of roentgenologic diagnosis is the determination of whether the sella is normal or not and the correlation of the roentgenological findings with the clinical status. An adequate diagnosis of the sella must take into account the following anatomical characters: (1) contour; (2) size; (3) form; (4) position; (5) contents; (6) roentgenological anatomy of the different portions of the sella and the surroundings; (7) the angles assumed by the anterior wall, the geometric axis, the dorsum, the clivus, and the entry to the sella. In addition, one must always keep in mind the normal and pathological variations possible. The normal variations may occur in so many different combinations that the normal sella is distinct for each individual, so to speak. It may indeed be possible that the roentgenologic characters of the sella may be useful in establishing a person's identity. The above anatomical characters are described in minute detail and pictured.

A comparison of the roentgenologic characters with the corresponding clinical data leads to the following conclusions. The size of the sella measured objectively conforms fairly well to the expected hypophyseal function (naturally after exclusion of tumor pressure, erosion, etc.). Alteration in the sella can also be established in cases in which direct hypophy-

seal symptoms are not clinically determinable (secondary hypophyseal change). In every suspected case of endocrine dysfunction therefore a sella examination should be undertaken. The size of the sella is, in general, closely correlated to the function and size of several vascular glands, especially the thyroid, parathyroids, etc., and not to just one. Alterations in the sella caused by changes in the cranial cavity are usually distinguishable roentgenologically from those due to changes in the hypophyseal region; but despite this a careful weighing of the clinical findings is highly desirable in differential diagnosis. The roentgenological differentiation of changes of the hypophysis and of the infundibular region is only academically possible but these are relatively rare so that the roengten findings must be taken in conjunction with the clinical in order to establish a differential diagnosis.

A morphological examination of the sella is a very useful aid and may even be diagnostic in (a) all endocrine examinations, especially the analysis of the functions of the different glands; (b) cases of suspected change in the skull and base of the skull (including involvement of the eye); (c) in a large variety of diseases like syphilis, pruritus, etc., and (d) constitutional examinations in which endocrine changes or any changes in the skull cavity or base of the skull are likely to occur.

Hassin, George B., Baker, E. L., and Wakefield, Howard. Roentgenographic bone changes in a second case of old poliomyelitis. *J. Am. M. Ass.*, July 25, 1925, lxxxv, 267–268.

In a previously reported case of old poliomyelitis the bones of the lower extremities exhibited changes almost paralleling those in the involved peripheral nerves and muscles. The paralysis in that case was of thirty-seven years' duration. In the second case here recorded the duration of the paralysis was fifty-nine years and affected only one extremity. A history is given of the case in a man aged sixty-one, examination of whom showed left cerebral thrombosis, combined with an old flaccid paralysis of the right lower extremity and bone changes peculiar to old cases of poliomyelitis.

The roentgen-ray examination showed a rather shallow acetabulum in the right hip and a slight lack of density of the bones of the corresponding lower extremity (lateral projection examination). The diameters of the tibia and fibula were greatly diminished, being scarcely greater than that of the medullary canal of normal size. The distal extremities of the tibia were practically normal in size. The affected bones also showed a smoothness and lack of the usual anatomic characteristics.

Heine, J. The significance of the transverse groove of the olecranon. *Fortschr. a. d. Geb. d. Röntgenstrahlen*, March, 1925, xxxiii, 206–207.

Since it is not always clear from the literature as to the precise location of the olecranon the following definition is given: The olecranon is the name given to that section of the ulna lying above (proximally to) the transverse groove, and which is bounded below (distally) by the coronoid process. The transverse groove appears roentgenologically in the lateral roentgenogram (ulnar-radial) as a small triangular rarefaction in the middle of the ulnar fork and is easily recognized. When the joint is roentgenographed in external extension with simultaneous strong supination, the lateral depression on the ulnar side shows up in the roentgenogram as a distinct rarefaction. There is some evidence pointing to a relationship between the transverse groove and the occurrence of transverse fractures of the olecranon.

Herman, Karl. Cholecystography. *Deutsche med. Wchnschr.*, Oct. 2, 1925, ii, 1665–1666.

Better results are obtained in the prone position than with the patient standing. Roentgenograms with the Bucky diaphragm cannot always be dispensed with, especially when the contrast material after an extended period has lost much of its contrasting power. The thicker the bile, the better is the picture observed. In hydrops of the gall-bladder the result may be negative because the thin cystic bile dilutes the bromine content of the hepatic bile to such an extent that contrasting power is lost.

Administration of 10 to 20 drops of tincture of opium three to four hours after the injection is useful in that it reduces the peristalsis of the bile ducts. The gall-bladder is often seen roentgenoscopically but not always. Films should be examined several times not only in illuminating boxes but also in clear daylight. Very frequently a repeated study of a supposedly negative film has resulted in the discovery of the gall-bladder shadow.

The reactions during injection are not very pronounced. Pain in the arm, edema, etc., which practically always occur are very inconvenient. It is best not to apply the Graham method in cases of icterus, heart disease, diabetes and nephritis.

Huber, O. The roentgen diagnosis of diaphragmatic hernia. *Deutsche med. Wchnschr.*, May 1, 1925, li, 729–730.

A typical case of large gastric hernia is described in which the roentgen finding made

the diagnosis possible. The patient had received a breast wound in 1915 from which he had recovered. In 1922 mild gastric symptoms had gradually developed to such an acute stage as to necessitate hospitalization. The roentgen examination showed an abnormally lifted diaphragm and a large stomach cavity. The diaphragm was difficultly movable and showed no inspiratory rise. Filling with barium showed an hour-glass stomach, both portions being about equal in size and connected by a narrow isthmus. No peristalsis was evident, nor could a definitely pyloric region be recognized. Although occasionally some of the contrast material flowed off, no activity of the antrum could be noticed. When the contrast material was very slowly swallowed it was noted that it descended to the lower portion of the stomach first and gradually a second upper shadow appeared, completely separate from the lower. Because of the condition of the patient it was not possible to try pressing the contents from the lower into the upper portion. These observations indicated that the upper portion of the stomach was located above the diaphragm. An apparent emptying from the lower portion was traced to the fact that the pyloric region passed back over the lower end of the stomach and thus gave a false picture. The diagnosis of diaphragmatic hernia was confirmed at operation.

HYMAN, ABRAHAM. Clinical and surgical aspects of renal neoplasms. *Surg., Gynec. & Obst.*, September, 1925, xli, 298–310.

A patient with classical symptoms of renal neoplasm, namely, pain, hematuria and tumor offers no diagnostic problem. The condition is manifest. Unfortunately, renal neoplasms may present such a protean clinical picture as to render the diagnosis most difficult. Despite the most careful application of all our resources we are occasionally left in doubt; and exploration of the kidney alone will make it possible to decide the issue. A series of 70 cases with hypernephroma predominating is discussed from the clinical standpoint.

Ordinary roentgenography by outlining the size and shape of the kidney will often prove of value in diagnosis. In 15 cases distinct enlargement and irregularity of the kidney outline was observed. In a few cases roentgenograms showed a perfectly normal kidney shadow and justified the exclusion of malignancy.

There is only one recognized form of treatment and that is nephrectomy. Radium and deep roentgen rays are to be used only as adjuvants. Deep roentgen therapy occasionally is of value in inoperable cases for controlling hematuria. Lumbar nephrectomy is the usual procedure. In the present series of 47 nephrectomies in adults there were 3 deaths, a mortality of 6 per cent. The prognosis in general is bad, death occurring from recurrence and cachexia, or metastases often as late as ten years after operation. The majority of deaths occur within two years following operation.

Of the patients surviving operation, 8 had been treated with roentgen rays or radium. Three of these had radium implanted deep into the wound near the pedicle soon after operation. The other five were treated after operation with deep roentgen-ray therapy. The patients so treated did not seem to do better and the percentage of lasting results was no higher than in the first series of 40 patients who were not treated with roentgen rays.

PRIBRAM, B. O., GRUNENBERG, K., and STRAUSS, OTTO. The roentgenologic demonstration of the gall-bladder and its clinical and practical significance. *Deutsche med. Wchnschr.*, Aug. 28, 1925, li, 1429–1432.

A direct roentgenologic demonstration of gallstones is such a rarity that it appears useless to make a roentgenogram of the gall-gladder region for that purpose alone.

The method of Graham is considered a very important advance in the roentgenology of the gall-bladder. It is possible to obtain a good picture of the gall-bladder with uniform density if the gall-bladder is emptied and efforts are made to prevent vomiting of the patient. If within sixteen to thirty hours a gall-bladder shadow does not appear or if an incomplete shadow is to be seen, it may be decided with great certainty that there is either an obstruction of the cystic duct or of the neck of the gall-bladder or else that the bladder is filled with concrements. In the many cases examined that have come to operation, there has not been a single one in which the roentgen finding led to a false diagnosis. Many times the roentgen picture was the only basis for judgment.

The technique followed is to clear the patient's gastrointestinal tract, and sixteen hours before the roentgen examination an intramuscular injection is given of 2 c.c. of hypophysin and 1 mg. atropin; ten to twenty minutes later a solution of 5 gm. of sodium tetrabromphenolphthalein in 40 c.c. of distilled water is very slowly injected at one sitting. The patient remains unfed until after the roentgen examination and should not be allowed to sit up. The roentgenograms are taken from the sixteenth to the twentieth hour with help of a Bucky diaphragm. The majority of patients tolerate the injection extremely well.

Very striking observations were made as to the position assumed by the gall-bladder in different cases. There is an extraordinary degree of variation in the location of the bladder. Not infrequently it was found against the spinal column as low as the fifth lumbar vertebra. Special emphasis is laid on the latter findings because such gall-bladders can produce definite symptoms characterizing what may be termed a pathological dropped bladder or cholecystoptosis. Such a set of symptoms may very readily simulate a chronic appendicitis. Very frequently such gall-bladders contained concretions.

When single stones are located in the gall-bladder and the cystic duct and neck of the bladder are free, filling of the gall-bladder may be good. When, however, very small concrements are located in the duct or neck of the bladder, the bladder itself may not be filled. Up to the present, the authors have not recorded a single failure in the roentgenologic diagnosis of occlusion of the cystic duct or of stones in the neck of the gall-bladder. An obstruction in the cystic duct or a gall-bladder full of concrements naturally prevents or retards entry of contrast material into the gall-bladder. Three cases illustrating these conditions are cited. Of especial interest is one case in which stenosis of the cystic duct caused by peritoneal adhesions was definitely diagnosed by this method. On the other hand, there is cited a case of subacute yellow atrophy of the liver in which the roentgen examination showed a normal gall-bladder that filled rather slowly. It is suggested that the method may be elaborated so as to constitute a procedure for studying liver function.

PROCTOR, OSCAR S. Chronic peptic ulcer in children. *Surg., Gynec. & Obst.*, July, 1925, xli, 63–69.

From the records of the last thousand gastric ulcers and from the last thousand duodenal ulcers seen at the Mayo Clinic it was found that 16 of the patients with gastric ulcer had symptoms dating back to childhood, even to the age of four or five years, and there were 26 with duodenal ulcer originating in childhood. Thus the onset of the disease in 21 out of every 1000 cases of peptic ulcer dates back to childhood. There seems little doubt that the disease is often unrecognized in children, and if the possibility of the condition is borne in mind there will be a steadily increasing number of cases diagnosed; and chronic peptic ulcer in children will cease to be a rarity.

Chronic or recurring attacks of dyspepsia in a child should lead one to consider the possibility of peptic ulcer, particularly if the growth is retarded or if the child is underweight or pale. Hyperchlorhydria is absent usually, and when present it may be helpful in diagnosis. Blood may be found in the gastric contents or in the stools, especially on repeated examination. The roentgen ray is of great assistance in diagnosis. Even among roentgenologists of wide experience few will make a definite diagnosis of peptic ulcer, but the fact that a lesion is present will usually be noted. In but few of the reported cases was roentgen exmination made but there is reason to believe that the findings are similar to those in the adult. The motility of the stomach is greater in children.

Medical treatment should always be thoroughly tried first. The younger the child, the more prompt the response to treatment. If medical treatment fails and if there is stenosis, repeated hemorrhage or perforation the case becomes surgical. One does not have to be concerned over the possibility of the ulcer being malignant or becoming so during childhood.

Only 19 cases have been found in the literature which could be regarded as chronic peptic ulcers in children, and 2 cases which are questionable. These are cited briefly and 3 cases observed at the Mayo Clinic are also reported.

REINBERG, SAM. A. The roentgen diagnosis of pulmonary cysticercosis. *Fortschr. a. d. Geb. d. Röntgenstrahlen*, April, 1925, xxxiii, 382–386.

It is stated definitely that the roentgenographic characteristics of pulmonary cysticerocosis are so highly characteristic as to be termed pathognomonic. This condition has been recognized in the living but twice, once by Jaksch-Wartenhorst, and once by the author.

The case described by the author occurred in a man aged twenty-nine. The roentgenographic examination disclosed the lung fields very clear and the hilic markings unchanged. In the upper parts of the lung fields there were seen circular isolated shadows, not very homogeneous. The single spherical shadows were of about the same size, 1.8 to 2 cm. in diameter. Their edges were sharply outlined and the surrounding lung tissue appeared unchanged without a sign of infiltration or edema. A total of 8 such shadows, 4 in each lung, was to be seen. Most of the shadows were located in the superficial portions of the lung near the pulmonary pleura. The lower lung fields were free of pathologic shadows.

Repeated roentgenographic examinations during the course of a year disclosed no changes in this picture, the number and localization of the shadows remaining the same. On the basis

of this finding the diagnosis of multiple pulmonary cysticercosis was made.

SCHELENZ, CURT. The roentgenologic demonstration of the bronchi by means of an iodine contrast material. *Deutsche med. Wchnschr.*, May 22, 1925, li, 870.

Being unable to obtain lipiodol, the author made use of a preparation manufactured locally from sesame oil. This product contained 37 per cent of combined iodine, and no free iodine. The material is brown in color, smells slightly of iodine and is rather viscous necessitating warming before injection. This material was injected into the trachea without preliminary local anesthesia because the material causes absolutely no irritation of the mucosa.

The preparation was observed roentgenoscopically to flow gradually down the trachea and into the bronchi. All observations indicate that the procedure is of value in demonstrating dilatations in the middle and lower portions of the lung, the upper lobes being rather difficult to reach. The method is a distinct advance in roentgen diagnosis of the lungs. Attention is directed to the work of Lynah of New York, who in 1922 suggested the filling of cavities in the lung with a bismuth oil. (The oily base in lipiodol is poppy-seed oil and not clove oil.)

RHEIN, JOHN H. W. Hypophysial pressure symptoms due to hydrocephalus causing cystlike distention of the third ventricle. *Arch. Neurol. & Psychiat.*, January, 1925, xiii, 71–79.

A case is described in a mentally deficient boy aged eighteen. The outstanding symptoms in this case were a moderate degree of adiposity, lowered sugar tolerance, anosmia, epileptiform convulsions and secondary atrophy of the optic nerve. The roentgenogram showed enlargement of the sella turcica which measured approximately 16 mm. long and 17 mm. deep. The floor of the sella was very thin. The posterior clinoid processes were destroyed, and the anterior clinoid processes were pushed forward and upward and very thin. There was no evidence of invasion characteristic of malignancy. The general appearance indicated a pressure effect, and the pressure evidently came from behind forward thereby destroying the posterior clinoid processes and pushing forward the anterior clinoid processes. A transphenoidal hypophysectomy was attempted, but the patient was in such poor condition that the operation was interrupted and the patient was returned to the ward, dying ten hours later. At autopsy the third ventricle was found transformed into a sac projecting downward in front of the pons, crowding the structures in this region and causing pressure atrophy. The fourth ventricle was also much distended. There was a small tumor on the under surface of the right cerebellar hemisphere; but the only symptom observed that was suggestive of cerebellar tumor was an inconstant tendency to fall backward.

In the discussion, Harvey Cushing points out that a cerebellar tumor in a young person quickly alters the outlines of the sella and one must not depend on those outlines for a localizing diagnosis. A suprasellar tumor in a child that might cause an internal hydrocephalus from occlusion of the foramen of Monro is apt to have calcareous depositions that are shown in the roentgenogram. An ordinary adenoma is not only rare in a child, but even in an adult rarely produces an internal hydrocephalus. The present case is merely a dilatation of the third ventricle which is an inevitable accompaniment of internal hydrocephalus and which sometimes may so balloon the third ventricle as to give the appearance of a cyst from below.

SIELMANN, RICHARD. Spontaneous pneumothorax due to athletic activity. *Fortschr. a. d. Geb. d. Röntgenstrahlen*, April, 1925, xxxiii, 363–366.

Spontaneous pneumothorax is considered mainly a concomitant of a tuberculous lung. There are, however, cases of unknown origin occurring in apparently healthy persons, in whom there is usually no exudate and after healing of a pneumothorax no disease of the lung can be demonstrated. Sneezing, laughing, bodily exertion and such like have been described as causative factors. A case is described in a man aged twenty-six who undertook a long distance run for the first time in several years. He finished the race despite stabs of pain in the left side, and pursued his work eight days longer without difficulty. He then complained of acute pain in the left thorax, and inability to get up. He was able to lie only on the right side; there was no fever, pulse was regular and somewhat accelerated. The patient was pale but showed no cyanosis. The roentgenogram showed a typical picture of acute pneumothorax of the left side. This condition was completely cured in three months by rest.

SISK, J. NEWTON. Osteitis fibrosa cystica. *Surg. Gynec. & Obst.*, October, 1925, xli, 481–489.

There is agreement that osteitis fibrosa cystica is a distinctly benign central lesion of the bone. The uniformly good results obtained by conservative surgery in such cases makes

this an important disease to be considered in cases of central bone lesion of questionable clinical course.

The result of roentgen-ray examination, while unsupported is not conclusive, yet it is reasonably characteristic and is a most reliable aid to diagnosis. The central bone lesions with cyst formation to be considered in making a presumptive diagnosis are osteitis fibrosa cystica, giant cell sarcoma, myxoma, chondroma, and sarcoma. These are eliminated by the rules of probability, the clinical facts, and the roentgen-ray findings. Between osteitis fibrosa cystica and giant cell sarcoma the difference can be as easily shown by the roentgenogram as the microscope. Some points of diagnostic importance in this particular are: longitudinal extent of enlargement of the shaft is more limited in giant cell sarcoma and the distention is greater. There is also usually no bowing of the shaft, while in osteitis fibrosa cystica the bowing is common and the cystic pockets are separated by trabeculae of compact bone and are clean cut, differing in this respect from sarcoma.

Next to the roentgenologic picture in diagnostic importance stands the clinical picture of osteitis fibrosa cystica, which in most cases is uniform and of long duration. The onset is in early life, trauma appears to be a common factor and the pathogenesis appears to be that of metaplasia and early malacia. Microscopic examination of tissue removed is essentially important in making a prognosis, if the signs of benignity or malignancy are definite; otherwise the postoperative clinical course is the only dependable basis for forming conclusions. The treatment is distinctly surgical at the time the lesion is recognized. The clinical histories in 6 cases are cited.

Sosman, Merrill C. Renal roentgenography during operation. *Surg., Gynec. & Obst.*, November, 1925, xli, 682–685.

Attempts to examine the kidney during operation using the head roentgenoscope (the operating room could not be darkened) were found unsatisfactory. The method was therefore modified to permit the use of a film small enough to be slipped into the operative wound behind and below the exposed kidney, the roentgenogram of the kidney being then made with the use of a small portable machine. The film is inclosed in a small rubber bag which has previously been sterilized and dried. Such a film can be developed, fixed and returned to the operating room in a few minutes and the surgeon can see for himself the exact location, size, number and character of the shadows. Ten minutes is the maximum time necessary to wheel up the machine, take the film, develop it and return it to the operating room. This is less time than the roentgenologist would use in preparing his retinae for roentgenoscopy. The procedure has a further advantage of furnishing a permanent record.

So far 25 cases have been thus examined. In 3 cases exposures were made to locate shadows thought to be calculi in the preoperative films and not found at operation. In all 3 the calculi were shown and were then localized and removed. In the 22 remaining cases all had had stones removed and the films were made to rule out the possibility of retained fragments. Four of these showed calculi remaining which were located and removed. So far not one of these patients has returned with a "recurrent stone." Six typical cases are briefly cited.

Teschendorf, Werner. The differential diagnosis of some normal and pathologic processes of the duodenum in the roentgenogram. *Deutsche med. Wchnschr.*, Aug. 28, 1925, li, 1432–1434.

With ordinary technique the normal duodenum can be demonstrated very readily. Its contours must be smooth and not appear broken through. In a person with pyloric spasm duodenal filling can usually be secured by having the patient lie upon the right side for about ten minutes, provided the stenosis is not an acute one. However, in certain cases suggesting not the least clinical sign of a pathologic process in the duodenum deviations from the smooth contour of the duodenum have been observed. These were cases examined in the lateral (Chaoul) position modified so that the upper portion of the body was higher than the lower. The upper duodenal region was well contrasted but certain plates showed a definite pulling out of the uppermost portion of the duodenum suggesting pericholecystic adhesions. There were, however, no clinical symptoms of such a condition. A study of the anatomical relations of the duodenum shows that this particular portion is the point of insertion of the hepatoduodenal ligament which carries the bile duct, hepatic artery and the portal vein. Consequently the pulling out of the upper portion of the duodenum was due in this case to the pull of the ligament and not necessarily to pathologic adhesions. In such cases a differential diagnosis in the upright position should be made. Contrary to general opinion it is believed there is no justification for concluding from the presence of a residual shadow in the duodenum after emptying of the stomach that there must be a pathologic process in the duodenum. In surfaces near the pylorus there

often occur barium deposits which produce a shadow of the bulbus adjacent to the pylorus. To clear up the doubt, it may be necessary to make another observation while the patient swallows a new barium suspension.

It is not always easy to distinguish an atonic duodenum from a duodenal dilatation caused by an obstruction. It is believed that the degree of kinking of the Kerkring valves in the filled portion of the duodenum gives a certain indication of the tonus of the duodenum. When a gas bubble is present there occurs relaxation of the circular and longitudinal musculature; and in meteorism, atonic gas-filled intestinal coils are present. Consequently a secondary atony of the duodenum may be due to presence of gas. This occurs relatively seldom. It is believed that when a duodenal gas bubble occurs in the definite absence of a stenosis there must be a certain atony of the bulbus duodeni, an atony that prevents the duodenal musculature from ejecting the gas bubble beyond the pars superior duodeni.

THOMS, HERBERT. Pelvimetry of the superior strait by means of the roentgen ray. *J. Am. M. Ass.*, July 25, 1925, lxxxv, 253–256.

Pelvimetry of the superior strait by roentgenographic methods is of distinct practical and scientific value in obstetrics. It should have a place in all obstetric clinics where teaching and classification of pelves is carried on. It has distant practical application in cases of suspected contraction of the superior strait, or those in which there is non-engagement of the fetal head at term. The measurement of the diameter of the superior strait in the living subject is accomplished more easily by roentgenographic methods than by any of the various procedures hitherto tried.

The roentgen-ray technique used for pelvic measurements is as follows: Duplitized super-speed films, double screen with Bucky-Potter diaphragm and a medium focus Coolidge tube are used, with target plate distance 36 in., point spark gap 7 in. (65 kv.) and 20 ma. The exposure is 16 to 30 sec., depending on the weight of the patient. It is essential that the target be placed over the center of the superior strait and that the plane of the superior strait be parallel to the sensitive plate underneath. In the living subject, it is possible to accomplish this by placing the patient in the semi-recumbent position with the back arched so that an imaginary line running from 1 cm. below the superior border of the symphysis posteriorly to the depression just below the spine of the fourth lumbar vertebra is exactly horizontal. The distance of the superior strait above the plate is measured with ordinary calipers and a notched lead strip previously calibrated for this particular height is inserted and the roentgenogram taken. After the relative distances of the various planes above the horizontal have been established and calibrated on different lead strips no further calculation becomes necessary, and the procedure becomes simply one of taking a roentgenogram. By means of the calipers, any diameter of the superior strait may be directly measured on the film and the distance read immediately on the scale produced by the notched lead strip.

VALLARINO, J. J. Preliminary report of the value of the roentgen ray in estimating the extent of amebic infection of the large intestine. *Am. J. Trop. Med.*, March, 1925, v, 149–156.

Defects in the large intestine were found in all cases of amebic infection due to *E. bistolytica* with definite symptomatology. These roentgen-ray findings checked up very well with the clinical findings in that the filling defects corresponded to the points of tenderness in the abdomen. The roentgenographic evidence furnished information of value in following the course of treatment. In some cases the findings on re-examination correlated well with the clinical improvement following treatment.

The defect observed in the majority of cases takes the form of a mottling of the affected part. The bowel loses its normal contour and a mottled area is found instead, the extent depending on the degree of the intestinal lesion. Particularly in old cases defects resembling obstructions are found which may be attributed to isolated patches of infected intestine.

The lesions are found mostly in the cecum and ascending colon up to the hepatic flexure. The next place in frequency is the sigmoid, and less often the transverse and descending colon. Better information is obtained when the opaque substance is administered by mouth than when a barium enema is given.

v. KOVÁTS, F. The roentgen diagonsis of bronchiectasis with the aid of "Lipiodol Lafay." *Deutsche med. Wchnschr.*, April 17, 1925, li, 653–654.

Bronchiectasis very frequently offers great diagnostic difficulties because certain forms, like the cylindrical, may escape detection. Lipiodol is claimed to be a sure aid in the diagnosis of bronchiectasis of all types.

The technique of examination is very simple. The larynx is locally anesthetized and 15 to 20 c.c. of warm lipiodol is dropped into the

larynx. Injection of lipiodol from the outside has also been recommended. The material is tolerated fairly well, and when the anesthesia has worn off the lipiodol is ejected, for the most part, in coughing.

Roentgenograms of bronchi thus obtained are extraordinarily striking in the richness of contrast and detail shown. A case is described in which the usual diagnostic methods merely suggested the probability of existence of bronchiectasis, whereas the lipiodol technique demonstrated it beyond a peradventure.

WILHELM, SEYMOUR F. Osteitis fibrosa and the hyperostotic form of bone syphilis. *Surg., Gynec. & Obst.*, November, 1925, xli, 624–639.

It is in the varying combination of the factors of destruction and repair that the great variations are to be noted in the anatomical and roentgenological pictures in bone and joint syphilis. There are at least gross morphological similarities between the clinical pictures of hyperostotic bone syphilis and osteitis fibrosa. The author, at the suggestion of Professor Pick, has examined the latter's large collection of pathological bone material in an effort to clear up the anatomical-pathological features of osteitis fibrosa and bone syphilis. The method of roentgenographing the macerated bones was utilized in this study.

In 3 cases of osteodystrophia fibrosa the chief characteristic of the anatomical and roentgenological findings is the complete absence of any periosteal participation. The second important feature is the state of the marrow cavity, which is markedly widened and may extend far into the epiphyses. The third important point is the appearance of the rebuilt bone substance. In the endosteal type of osteitis fibrosa it is finely spongious and densely porous, being of greater density in the tibia than in the fibula. In senile osteitis fibrosa with sabre tibiae the rebuilt corticalis is generally compact but traversed by numerous cracks parallel to the outer surface. There is a lamellation of the corticalis which is very characteristic in the roentgenogram.

For comparison, the anatomical and roentgen pictures in 4 syphilitic tibiae are presented. The roentgenogram shows beautifully the marked degree to which the periosteum participates in the deforming, new bone building processes. No other method of gross or microscopic examination is quite as good. In addition to the marked often tremendous participation of periosteum there is to be found a more or less advanced narrowing and obliteration of the marrow cavity and a sclerotic or finely porous quality of the newly built bone tissue. The meshes or porous part in the roentgen pictures seem to be directed lengthwise parallel to the long axis of the diaphysis. The sabre blade or sabre shaft form of the tibia in syphilis may be due to the periosteal new formation of bone; or to an osteitic rebuilding and elongation. The sabre blade tibia of Paget's disease is the result of the rebuilding and elongation of the bone.

The occurrence of more or less well formed cysts or of single circumscribed dense foci accompanying a diffusely spreading osteitic new bone formation are diagnostic points in favor of osteitis fibrosa as against syphilis. In the remaining still doubtful cases additional clinical methods should be employed to arrive at a diagnosis.

ROENTGEN AND RADIUM THERAPY

SCHOLTEN, GUSTAV C. J., and VOLTZ, FRIEDRICH. The radiation treatment of gynecological carcinoma. *München. med. Wchnschr.*, Jan. 2, 1925, lxxii, 6–10.

The results obtained in the Munich Frauenklinik are summarized. Exclusive treatment with radioactive substances was given in 755 cases of collum carcinoma and 103, or 13.2 per cent were pronounced cured after five years. There were 110 operable cases with 48 cures; 136 borderline cases with 31 cures; 340 inoperable cases with 23 cures; and 169 hopeless cases with one cure. These figures refer to cases treated up to 1917. The figures for the years 1918 and 1919 show essentially the same levels. The evidence is quite clear that exclusive radiation treatment of gynecological carcinoma as expressed by the statistics in large series of cases is a distinctly justified mode of therapy. Since 1922 the clinic has gone over to the use of larger fields and greater skin-focal distance in roentgen therapy. It is emphasized that the roentgen therapy was always applied as a complementary treatment to the treatment with radioactive substances.

A new element in the technique of treatment has been the introduction of irradiation of the hypophysis. Since 1923 all the cases in this clinic (more than 200) received a pre-irradiation of the hypophysis. Although not enough time has elapsed for a final judgment as to the value of this procedure, it is quite definite that pre-irradiation of the hypophysis was at least in no case injurious. There are certain indications that many cases thus treated were favorably influenced.

In discussing deep roentgen therapy it is mentioned in passing that the few cases of roentgen sickness observed in this clinic were

due in the opinion of the authors, to psychic effects. The technique of hypophysis irradiation is two fields, 6 by 8 cm., skin focal distance 30 cm., each field receiving 50 per cent of a skin erythema dose.

The three factors involved in radiation therapy are the physical foundations, the biological reaction of the cells and therapeutic management. The physical factors are today fairly well worked out. These must be known and understood by anyone attempting radiation therapy. The biological reaction is still under investigation and controversy; and the therapeutic management must always be dependent upon our knowledge of the physical fundamentals and the biological processes. Only those statistical figures which are based upon a large material can suggest to us the direction in which therapeutic management can develop and improve.

SIMONS, ALBERT. Treatment of chronic ulcerating fistulas with thorium X. *Deutsche med. Wchnschr.*, Jan. 16, 1925, li, 109.

Thorium X needles find a useful application in the treatment of chronic ulcerating fistulas due to various causes. A case is reported in a woman sixty years old with a questioned diagnosis of osteosarcoma of the orbital rim. Following radium treatment, this tumor receded promptly but left a small pinhole fistula leading directly to the bone. Repetition of radium irradiation yielded no result nor did other medication. Finally a thorium X needle 2 cm. long with an activity of one mc. emanation was pushed into the fistula opening and after fourteen days the purulent discharge decreased considerably. Two months later another treatment of 1.5 mc. thorium X was applied in the same manner; and the patient has remained free of symptoms for the past four months.

Tuberculous fistulae of the neck glands likewise yielded to 0.5 to 1.0 mc. thorium X, healing occurring in two to four weeks. The thorium needles may be allowed to remain in the fistula for several days; their activity lasts only about three or four weeks.

SMITH, LAWRENCE W., et al. Treatment of pertussis by roentgen ray. *J. Am. M. Ass.*, July 18, 1925, lxxxv, 171–177.

A summary is given of the outstanding clinical and laboratory findings in 850 cases of pertussis treated by roentgen radiation and observed through the whooping cough clinic of the Boston Floating Hospital. All evidence is unanimous that roentgen therapy is of value in reducing the number and severity of the paroxysms and in shortening the duration of the disease. The mechanism by which the clinical improvement takes place is as yet unknown, but it is believed to be due to a diminution in the nervous reflex from the pressure of the hilum lymph nodes by a reduction in their size. There may also be some effect on the blood serum as has been suggested in relation to the etiology of the convulsions in the more severe cases. The greatest benefit from the roentgen treatment occurs in the paroxysmal stage, and especially in the younger patients. Most of the patients (499) presented themselves for treatment during the paroxysmal stage.

It has been suggested that a possible harmful effect of the roentgen rays may be exerted on the thymus and on the thyroid, but the doses are ordinarily so small, that it does not seem possible that any damage of physiologic significance can be caused, especially as the entire dose is considerably less than a skin erythema dose.

The importance of early diagnosis is emphasized and such a diagnosis should be possible in a majority of the cases from a combination of bacteriologic, hematologic and roentgenologic examinations in conjunction with adequate history. It should be possible ultimately to provide for the vaccination against whooping cough of all infants, beginning from the third to the sixth month of life. This prophylactic vaccination should be repeated yearly for the first three or four years, which represent the years in which practically the entire mortality from whooping cough occurs.

MISCELLANEOUS

ANDRASSY, KARL. Hard ray snapshot versus time exposure. *Fortschr. a. d. Geb. d. Röntgenstrahlen*, April, 1925, xxxiii, 391–392.

The technique employing hard rays is suitable where first consideration is shortening of the time of exposure: as for instance in the case of children. It is also of advantage in demonstrating the fine structure in bones because intensifying screens may be dispensed with.

It was found however that the finest structures could be demonstrated with the same accuracy when employing soft radition. The essential point is knowledge of the exact time of exposure. In order to attain this end with objects of medium thickness, approximately 10 to 12 cm., a Bucky-Potter diaphragm should be employed. There is evidence that roentgen films from different manufacturers respond differently according to the hardness of the radiation. It is concluded that for "ordinary" cases employment of the customary roentgeno-

graphic technique with suitable variation in the tube voltage is an ample and rational procedure.

BELLUCCI, BRUNO. Changes in blood pressure from irradiation of the testicles in old men. *Arch. di radiol.*, May-June, 1925, i, 377–381.

With the object of determining the effect of lack of the harmones produced by seminiferous tissue and leaving intact the secretion of interstitial tissue the author irradiated the testicles of old men who were approaching the end of their sexual life. Roentgen rays are known to have an elective destructive action on seminiferous cells while they leave interstitial cells intact. All of the subjects were men over sixty years of age with a pressure of more than 180 mm.; they were afebrile and of course were not given any drug during the treatment that could affect blood pressure. They were irradiated on a single anterior field covering the two testicles, spark gap 38 cm., filter 5 mm. aluminum, focal distance 23 cm. The dose given at one sitting was about 5 H. Blood pressures were taken every day with a Pachon oscillometer and the pulse counted.

There was always a reduction of maximum pressure which reached its maximum about ten days after the irradiation, and was in some cases as much as 100 mm. This was preceded by a temporary increase which reached its maximum about four days after irradiation and was followed by a sudden fall. There was also a temporary rise of minimum pressure for four days and then a fall which reached its maximum in ten days after irradiation. The number of pulsations either remained unchanged or increased slightly, the line for the pulse count sometimes crossing that for maximum pressure.

To prove that decreased pressure was due to the lack of testicle hormone the author gave extract of testicle in three of the cases at the moment of greatest decrease and the pressure rose in three or four hours after it was given. In the untreated case the maximum pressure began to rise in twenty or twenty-five days after the irradiation and gradually resumed its original height.

The question arises as to whether the fall of pressure was due to the lack of seminiferous hormone or to the fact that in its absence the interstitial hormone predominated. It has also been suggested that the lack of seminiferous hormone brings about an increase of thyroid hormone, which is known to increase heart action and blood pressure. The author believes that undoubtedly the fall in pressure is due to lack of seminiferous hormone, which acts directly or indirectly on the vasomotor system, almost certainly through the sympathetic. In the male climacteric, as in the female, though to a lesser degree, there is great liability of the vegetative nervous system.

It seems strange that the rays would cause a fall of pressure when the pressure generally rises with the termination of sexual life, and in view of the fact that some authors have brought about a fall of blood pressure by giving extract of testicle. But the fact remains that the results were definite and constant, and the author suggests the use of roentgen rays for those patients who in the climacteric begin to have disequilibrium of the endocrine system with hypertension.

BERNHARD, FRIEDA. Roentgen-ray irradiation of the spleen and blood coagulability. *Arch. f. klin. Chir.*, 1924, CXXX, 93–109.

The spleen is not the organ governing coagulability of the blood. Only about one in three persons receiving irradiation of the splenic region responds with a reduction in the coagulation time of the blood. The results of the treatment are the same in persons who have undergone a splenectomy as in normal individuals.